09743827

Connecting via Winsock to STN

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LOGINID:ssspta1613sxw

PASSWORD:
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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
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NEWS 3	Feb 24	PCTGEN now available on STN
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FILE 'HOME' ENTERED AT 14:36:03 ON 01 AUG 2003

=> fil casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CASREACT' ENTERED AT 14:36:15 ON 01 AUG 2003
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTENT:1907 - 27 Jul 2003 VOL 139 ISS 4

Some records from 1974 to 1991 are derived from the ZIC/VINITI data file and provided by InfoChem and some records are produced using some INPI data from the period prior to 1986.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Crossover limits have been increased. See HELP RNCROSSOVER for details.

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

=>
Uploading 09743827f.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 14:36:41 FILE 'CASREACT'
SCREENING COMPLETE - 13 REACTIONS TO VERIFY FROM 3 DOCUMENTS

100.0% DONE 13 VERIFIED 10 HIT RXNS 3 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 44 TO 476
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1 (10 REACTIONS)

=> s l1 full
FULL SEARCH INITIATED 14:36:46 FILE 'CASREACT'
SCREENING COMPLETE - 1267 REACTIONS TO VERIFY FROM 81 DOCUMENTS

100.0% DONE 1267 VERIFIED 752 HIT RXNS 48 DOCS
SEARCH TIME: 00.00.02

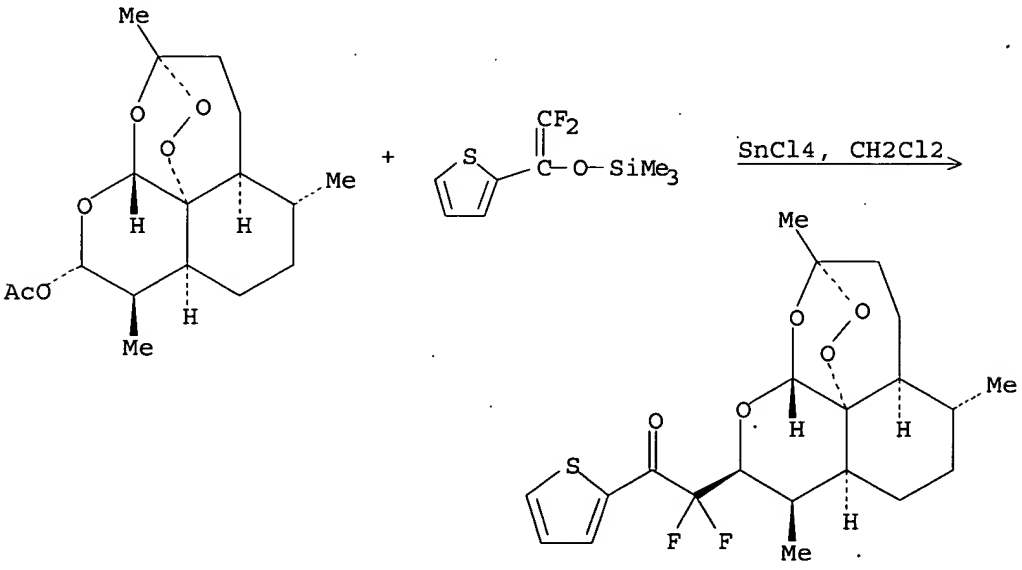
L3 48 SEA SSS FUL L1 (752 REACTIONS)

=> s l3 and lewis acid
6247 LEWIS
140951 ACID
4424 LEWIS ACID
(LEWIS(W)ACID)
L4 4 L3 AND LEWIS ACID

=> d l4 1-4

L4 ANSWER 1 OF 4 CASREACT COPYRIGHT 2003 ACS on STN

RX(4) OF 4

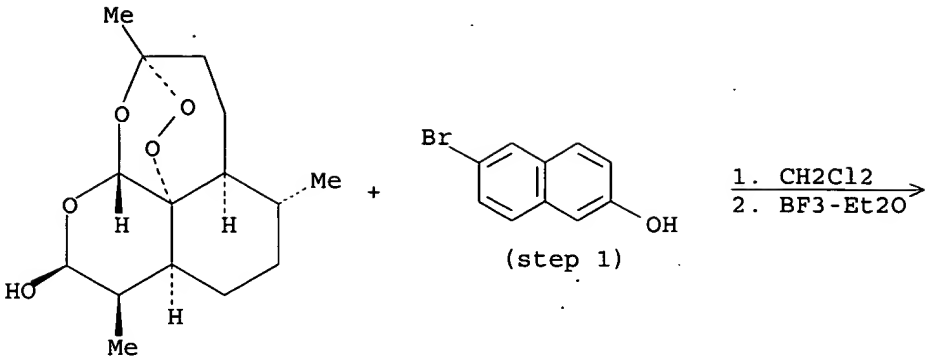


stereoisomers
29%

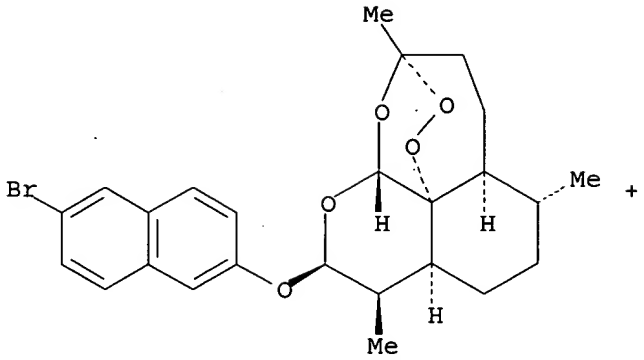
REF: Journal of Organic Chemistry, 66(23), 7858-7863; 2001

L4 ANSWER 2 OF 4 CASREACT COPYRIGHT 2003 ACS on STN

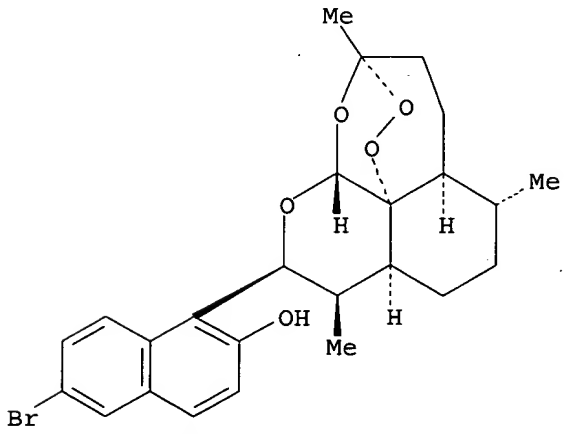
RX(1) OF 3



RX(1) OF 3



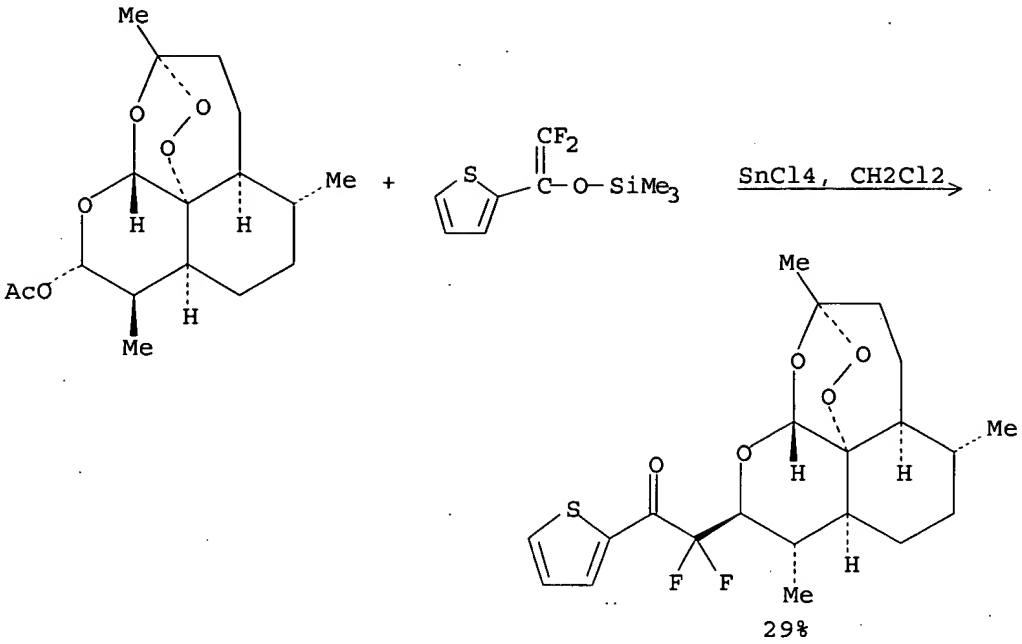
RX(1) OF 3



REF: Tap Chi Hoa Hoc, 38(4), 92-95; 2000
NOTE: mol. sieves used

L4 ANSWER 3 OF 4 CASREACT COPYRIGHT 2003 ACS on STN

RX(4) OF 4

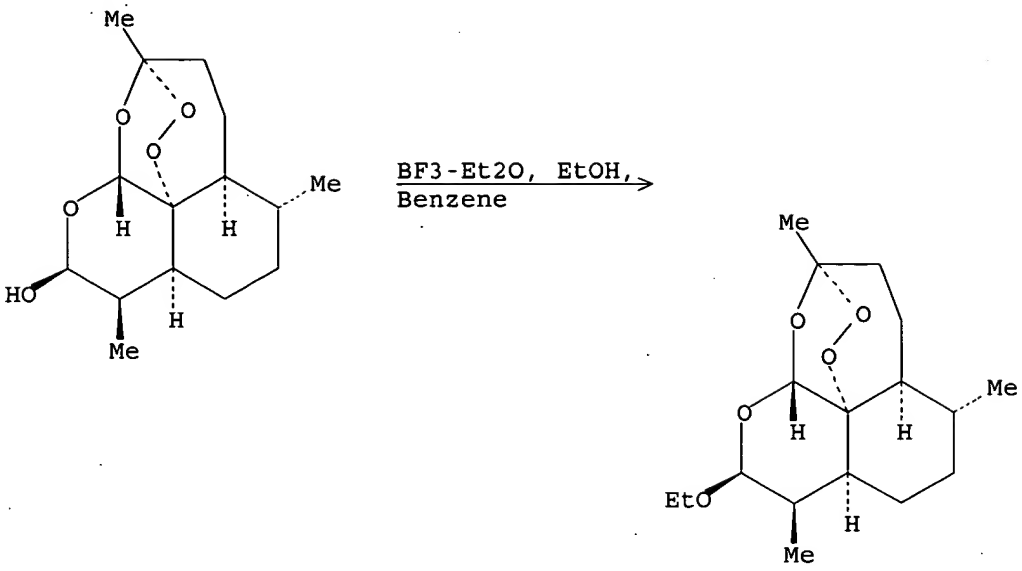


REF: Tetrahedron Letters, 42(8), 1487-1489; 2001

NOTE: stereoselective

L4 ANSWER 4 OF 4 CASREACT COPYRIGHT 2003 ACS on STN

RX(2) OF 16



stereoisomers

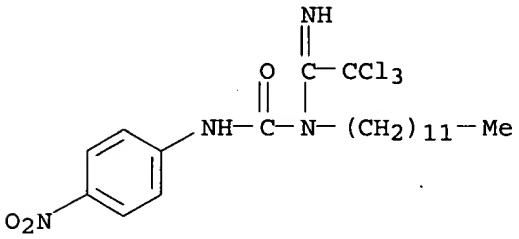
72%

REF: Journal of Medicinal Chemistry, 31(3), 645-50; 1988

```
=> s trichloroacetimidoyl
L3          84 TRICHLOROACETIMIDOYL

=> d l3

L3   ANSWER 1 OF 84  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   96167-65-6  REGISTRY
CN   Urea, 1-dodecyl-3-(p-nitrophenyl)-1-(2,2,2-trichloroacetimidoyl)-
     (7CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C21 H31 Cl3 N4 O3
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS
         (*File contains numerically searchable property data)
```



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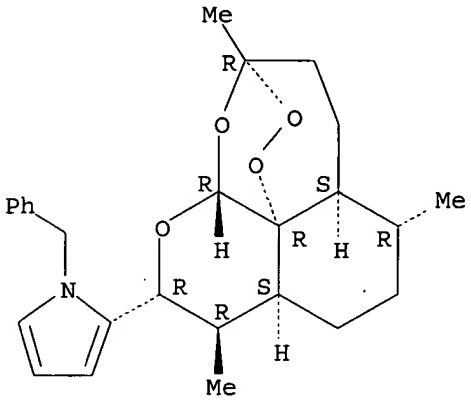
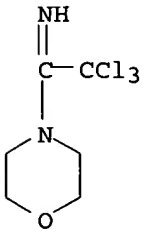
```
=> s deoxoartemisinin
L4          21 DEOXOARTEMISININ

=> d l4

L4   ANSWER 1 OF 21  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   220114-98-7  REGISTRY
CN   1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-
     3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   10.alpha.-(1-Benzylpyrrol-2-yl)-10-deoxoartemisinin
FS   STEREOSEARCH
MF   C26 H33 N O4
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.  Rotation (+).
```



L1 ANSWER 50 OF 84 REGISTRY COPYRIGHT 2003 ACS on STN
RN 35891-13-5 REGISTRY
CN Morpholine, 4-(2,2,2-trichloro-1-iminoethyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Morpholine, 4-(2,2,2-trichloroacetimidoyl)- (6CI)**
FS 3D CONCORD
MF C6 H9 Cl3 N2 O
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS
(*File contains numerically searchable property data)



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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:11:54 ON 31 JUL 2003

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:12:06 ON 31 JUL 2003
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 29 JUL 2003 HIGHEST RN 557055-78-4
DICTIONARY FILE UPDATES: 29 JUL 2003 HIGHEST RN 557055-78-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

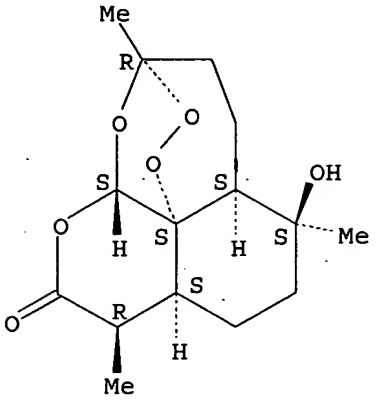
Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s artemisinin
L1 91 ARTEMISININ

=> d l1

L1 ANSWER 1 OF 91 REGISTRY COPYRIGHT 2003 ACS on STN
RN 463305-57-9 REGISTRY
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10(3H)-one, octahydro-6-hydroxy-3,6,9-trimethyl-, (3R,5aS,6S,8aS,9R,12S,12aS)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **(+)-10.beta.-Hydroxyartemisinin**
FS STEREOSEARCH
MF C15 H22 O6
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1947 TO DATE)
1 REFERENCES IN FILE CAPLUS (1947 TO DATE)

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LOGINID:ssspta1613sxw

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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FILE 'HOME' ENTERED AT 14:40:55 ON 31 JUL 2003

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:41:03 ON 31 JUL 2003
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STRUCTURE FILE UPDATES: 29 JUL 2003 HIGHEST RN 557055-78-4
DICTIONARY FILE UPDATES: 29 JUL 2003 HIGHEST RN 557055-78-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

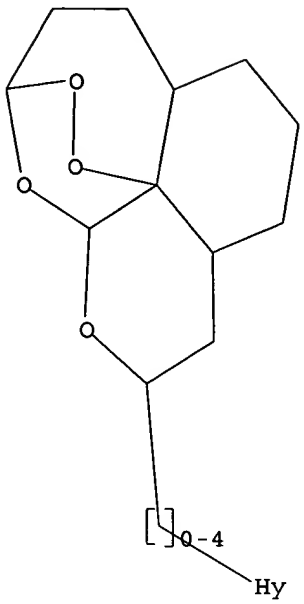
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09743827d.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 sss sam
SAMPLE SEARCH INITIATED 14:41:19 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     98 TO ITERATE

100.0% PROCESSED      98 ITERATIONS                                5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         1367 TO     2553
PROJECTED ANSWERS:               5 TO      234

L2             5 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 14:41:23 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1996 TO ITERATE

100.0% PROCESSED    1996 ITERATIONS                              96 ANSWERS
SEARCH TIME: 00.00.01

L3            96 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   148.15     148.36

FILE 'CAPLUS' ENTERED AT 14:41:27 ON 31 JUL 2003
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
```

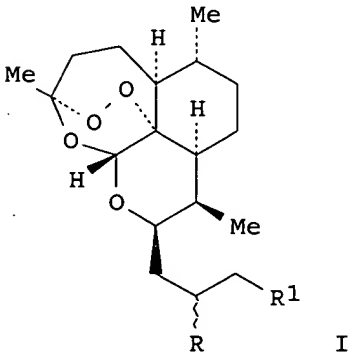
FILE COVERS 1907 - 31 Jul 2003 VOL 139 ISS 5
FILE LAST UPDATED: 30 Jul 2003 (20030730/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3 full
L4 26 L3

=> d l4 1-26 ibib abs hitstr

L4 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:162541 CAPLUS
DOCUMENT NUMBER: 138:401919
TITLE: Discovery of the anti-malarial activity of new derivatives of artemisinin
AUTHOR(S): Nguyen, Van Tuyen; Tran, Khac Vu; Tran, Van Sung; Pham, Van Cuong; Mai, Van Tri
CORPORATE SOURCE: Institute of Chemistry, National Center for Science and Technology, Vietnam
SOURCE: Tap Chi Hoa Hoc (2002), 40(2), 124-126
CODEN: TCHHDC; ISSN: 0378-2336
PUBLISHER: Toa Soan Tap Chi Hoa Hoc
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

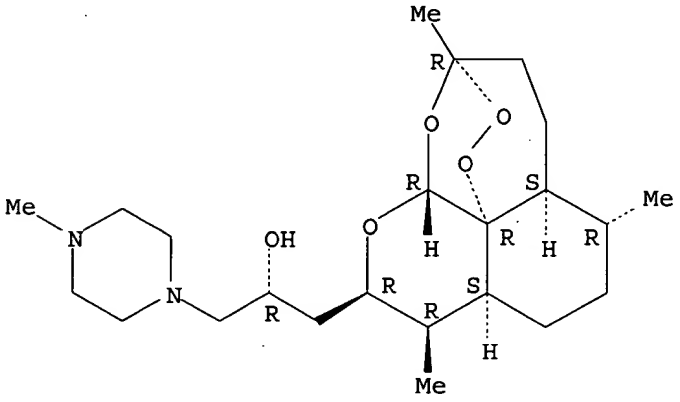
AB Synthesis and art malarial activity of a no. of new of 12-deoxoartemisinin amine derivs. I [R = .alpha.-, .beta.-OH; R1 = NEt2, NH(CH2)Ph,

N(Me)CH2Ph, 4-methyl-1-piperazinyl, 4-methyl-1-piperidinyl, 4-phenyl-1-piperidinyl, pyridinylamino] were presented.

IT **530739-37-8P 530739-38-9P 530739-39-0P 530739-40-3P 530739-41-4P 530739-42-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and anti-malarial activity of amine derivs. of artemisinin)

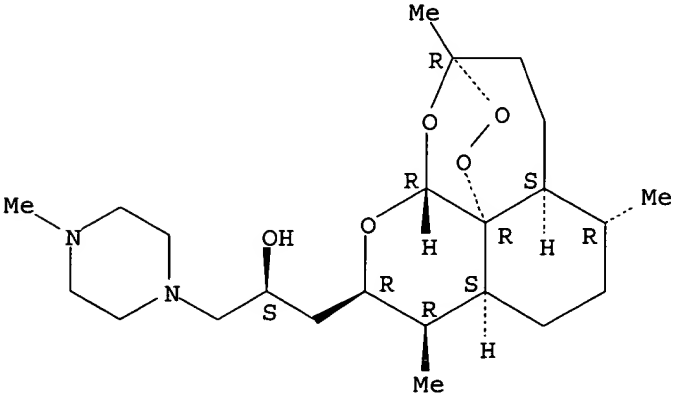
RN 530739-37-8 CAPLUS
CN 1-Piperazineethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-4-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



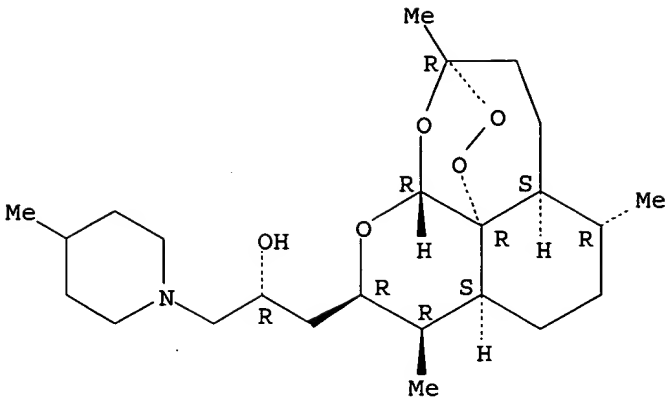
RN 530739-38-9 CAPLUS
CN 1-Piperazineethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-4-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



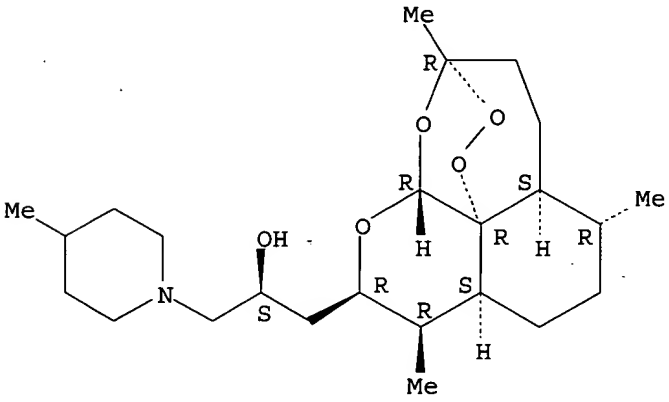
RN 530739-39-0 CAPLUS
CN 1-Piperidineethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-4-methyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



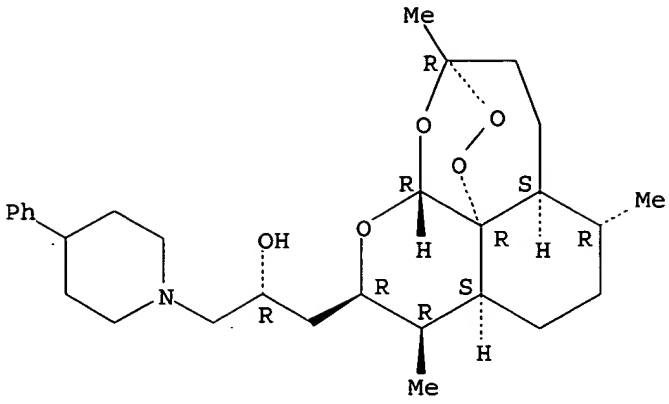
RN 530739-40-3 CAPLUS
CN 1-Piperidineethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-4-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



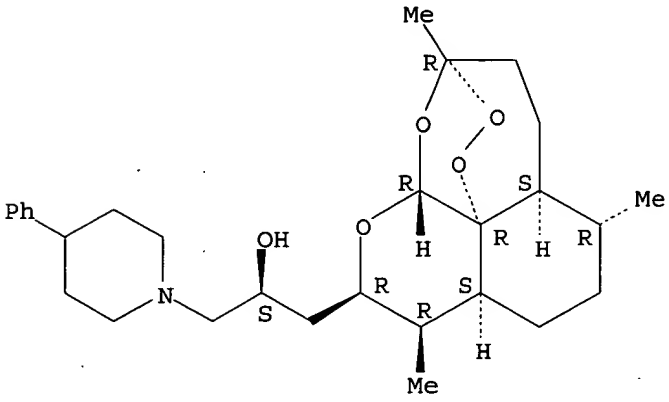
RN 530739-41-4 CAPLUS
CN 1-Piperidineethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-4-phenyl-, (.alpha.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



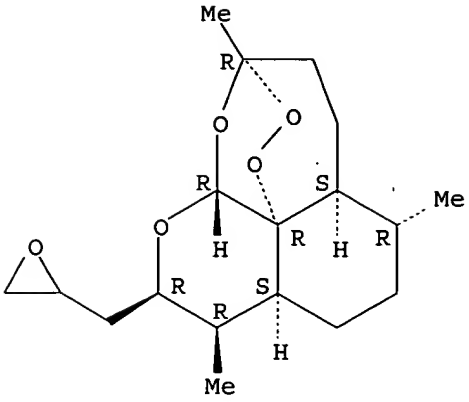
RN 530739-42-5 CAPLUS
CN 1-Piperidineethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-4-phenyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **194409-61-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and anti-malarial activity of amine derivs. of artemisinin)
RN 194409-61-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(oxiranylmethyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN

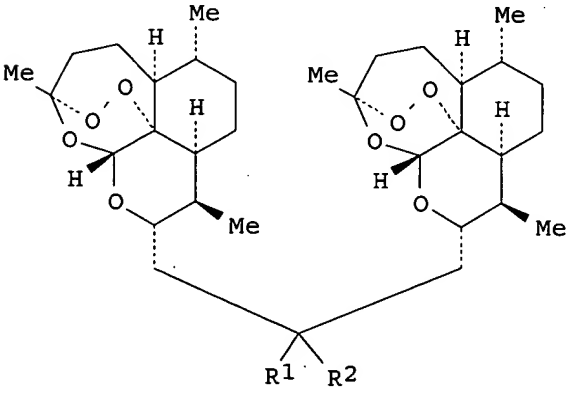
ACCESSION NUMBER: 2003:120372 CAPLUS
DOCUMENT NUMBER: 138:304415

TITLE: Orally Active, Antimalarial, Anticancer, Artemisinin-Derived Trioxane Dimers with High Stability and Efficacy

AUTHOR(S): Posner, Gary H.; Paik, Ik-Hyeon; Sur, Surojit; McRiner, Andrew J.; Borstnik, Kristina; Xie, Suji; Shapiro, Theresa A.
CORPORATE SOURCE: Department of Chemistry, School of Arts and Sciences, The Johns Hopkins University, Baltimore, MD, 21218-2685, USA

SOURCE: Journal of Medicinal Chemistry (2003), 46(6), 1060-1065
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

GI



II

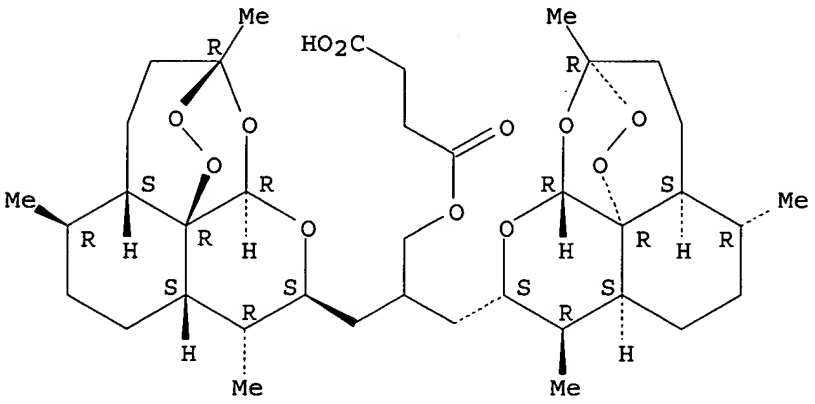
AB In only two steps and in 70% overall yield, naturally occurring trioxane artemisinin (I) was converted on a gram scale into C-10-carba trioxane

dimer II (R1R2 = CH2). This new, very stable dimer was then transformed easily in one addnl. step into four different dimers II [R1 = H, R2 = CH2OH (III); R1 = OH, R2 = CH2OH (IV); R1R2 = CH2O; R1R2 = O (V)]. Alc. and diol dimers III and IV and ketone dimer V are 10 times more antimalarially potent in vitro than I, and alc. and diol dimers III and IV are strongly growth inhibitory but not cytotoxic toward several human cancer cell lines. Water-sol. carboxylic acid derivs. II [R1 = CH2OCOCH2CH2CO2H, R2 = H (VI)] and II [R1 = CH2OCOCH2CH2CO2H, R2 = OH (VII)] were easily prepd. in one addnl. step from dimers III and IV. Carboxylic acid dimers VI and VII are thermally stable even at 60 .degree.C for 24 h, are more orally efficacious as antimalarials in rodents than either artelinic acid or sodium artesunate, and are strongly inhibitory but not cytotoxic toward several human cancer cell lines.

IT **509092-58-4P 509092-59-5P 509092-64-2P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., stability, antimalarial and anticancer activity of artemisinin-derived trioxane dimers)

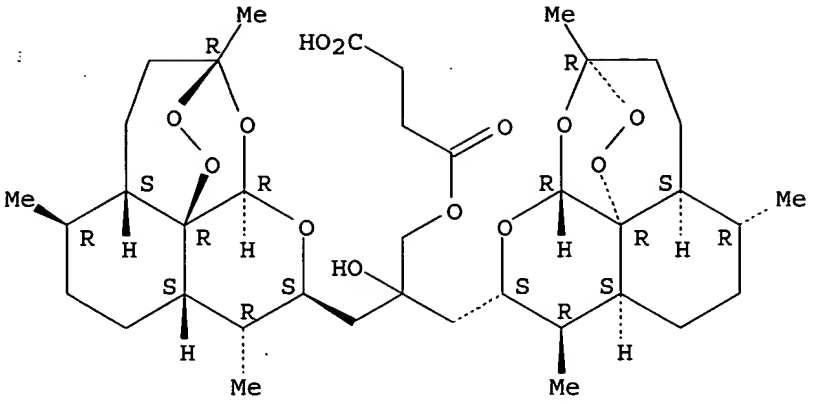
RN 509092-58-4 CAPLUS
CN Butanedioic acid, mono[3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]propyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



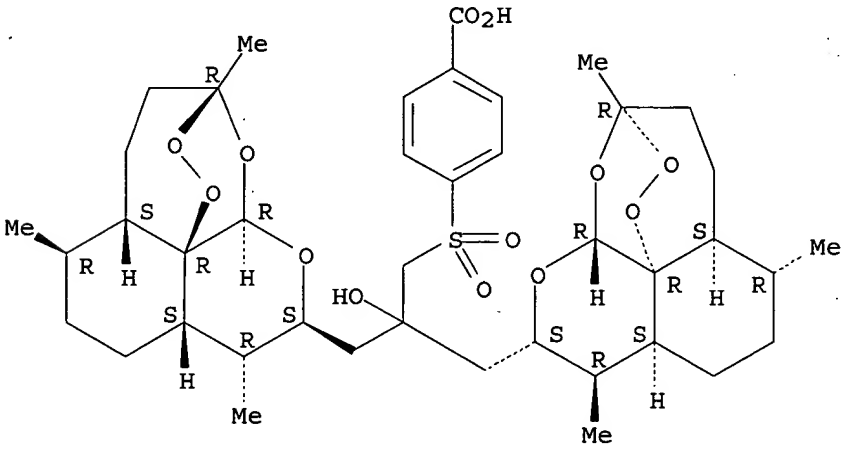
RN 509092-59-5 CAPLUS
CN Butanedioic acid, mono[3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-2-hydroxypropyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



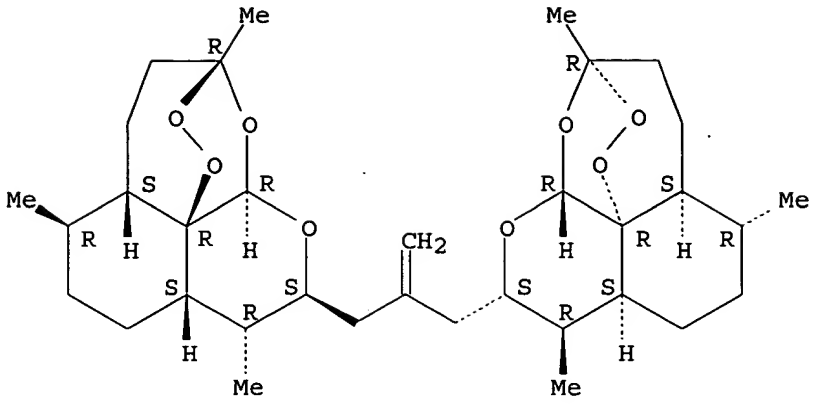
RN 509092-64-2 CAPLUS
CN Benzoic acid, 4-[[3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-2-hydroxypropyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



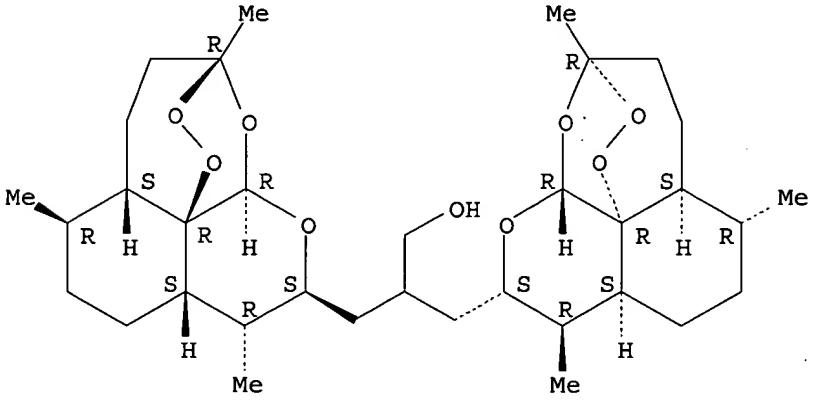
IT **509092-53-9P 509092-54-0P 509092-55-1P**
509092-56-2P 509092-57-3P 509092-60-8P
509092-61-9P 509092-63-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., stability, antimalarial and anticancer activity of artemisinin-derived trioxane dimers)
RN 509092-53-9 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10,10'-(2-methylene-1,3-propanediyl)bis[decahydro-3,6,9-trimethyl-, (3R,3'R,5aS,5'aS,6R,6'R,8aS,8'aS,9R,9'R,10S,10'S,12R,12'R,12aR,12'aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



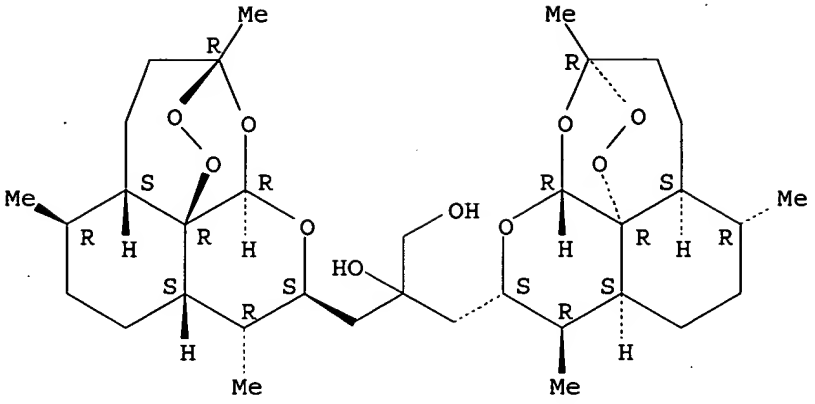
RN 509092-54-0 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-propanol, .beta.-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10S,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 509092-55-1 CAPLUS
CN 1,2-Propanediol, 3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]- (9CI) (CA INDEX NAME)

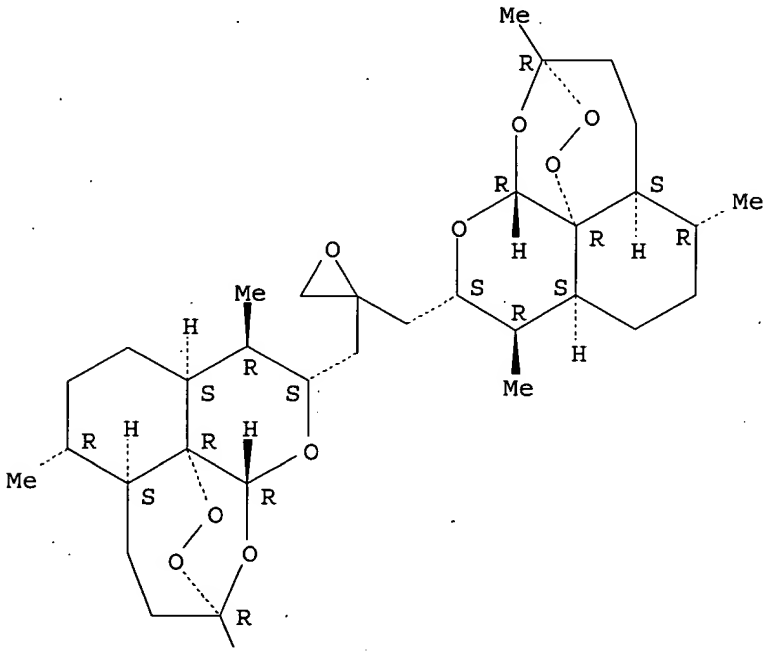
Absolute stereochemistry.



RN 509092-56-2 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10,10'-[oxiranylidenebis(methylene)]bis[decahydro-3,6,9-trimethyl-, (3R,3'R,5aS,5'aS,6R,6'R,8aS,8'aS,9R,9'R,10S,10'S,12R,12'R,12aR,12'aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

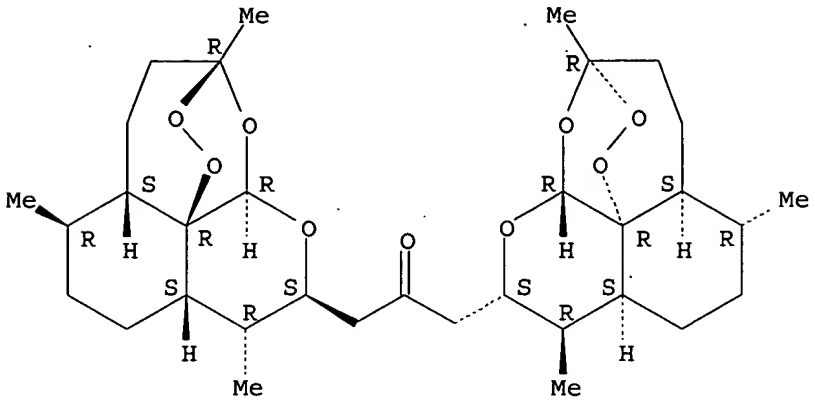
PAGE 1-A



PAGE 2-A

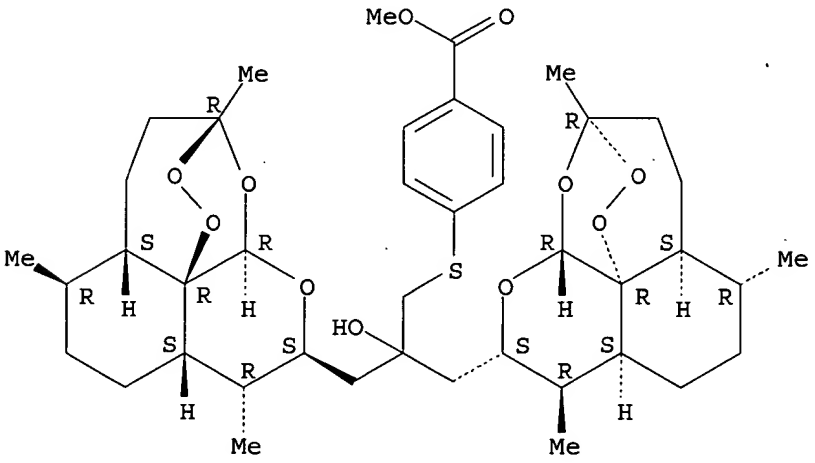
RN 509092-57-3 CAPLUS
CN 2-Propanone, 1,3-bis[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



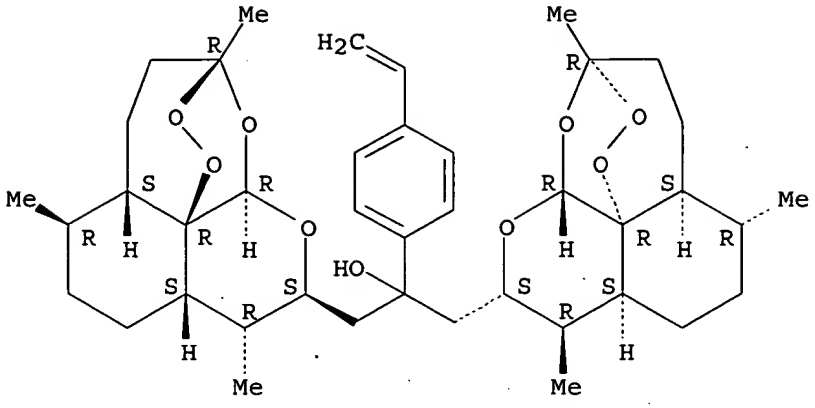
RN 509092-60-8 CAPLUS
CN Benzoic acid, 4-[[3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-2-hydroxypropyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



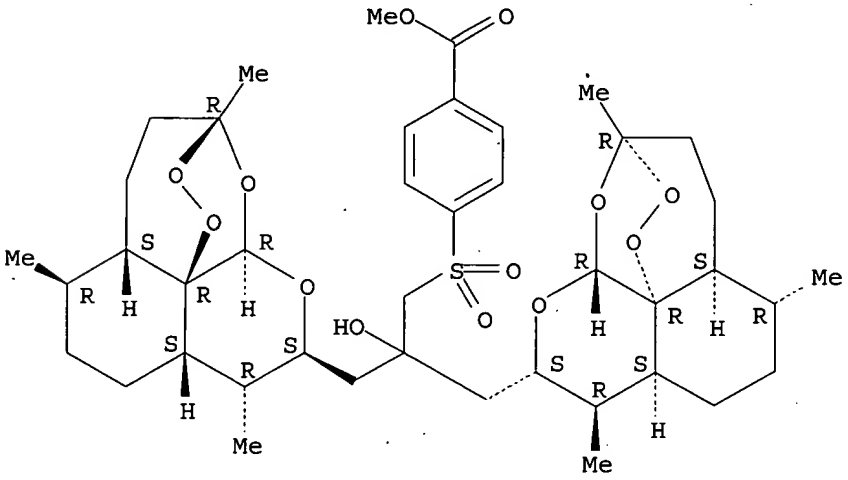
RN 509092-61-9 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ethanol, .alpha.-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-.alpha.-(4-ethenylphenyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10S,12R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



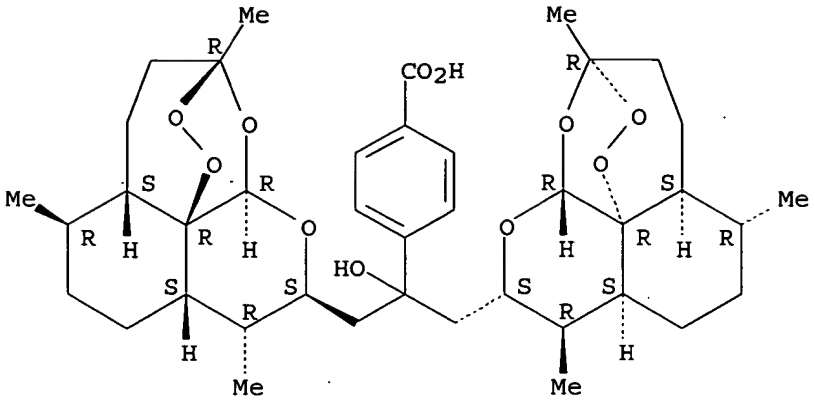
RN 509092-63-1 CAPLUS
CN Benzoic acid, 4-[[3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-2-hydroxypropyl]sulfonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



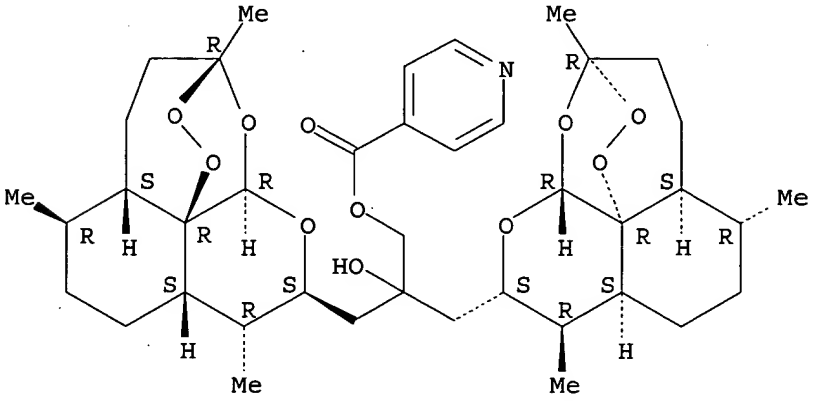
IT **509092-62-0P 509092-65-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., stability, antimalarial and anticancer activity of artemisinin-derived trioxane dimers)
RN 509092-62-0 CAPLUS
CN Benzoic acid, 4-[[2-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-[[(3R,5aS,6R,8aS,9R,10S)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-1-hydroxyethyl]thio]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



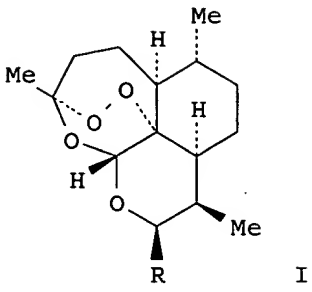
RN 509092-65-3 CAPLUS
CN 4-Pyridinecarboxylic acid, 3-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2-[[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]methyl]-2-hydroxypropyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:940354 CAPLUS
DOCUMENT NUMBER: 138:170369
TITLE: Synthesis of new nitrogen-containing 12-deoxoartemisinin derivatives
AUTHOR(S): Tran, Van Sung; Tran, Khac Vu; Nguyen, Van Tuyen
CORPORATE SOURCE: Inst. of Chem., National Center for Natural Science and Technol. of Vietnam, Vietnam
SOURCE: Tap Chi Hoa Hoc (2002), 40(3), 62-65
CODEN: TCHHDC; ISSN: 0378-2336
PUBLISHER: Toa Soan Tap Chi Hoa Hoc
DOCUMENT TYPE: Journal
LANGUAGE: Vietnamese
OTHER SOURCE(S): CASREACT 138:170369
GI



I

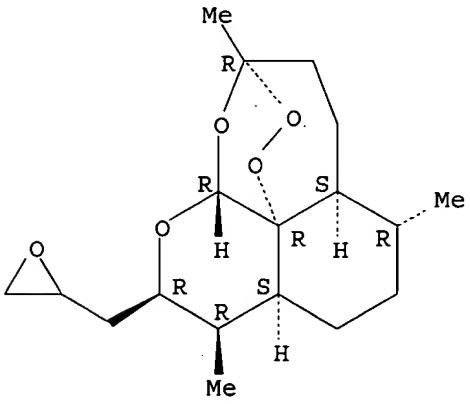
AB New nitrogen-contg. 12-deoxoartemisinin derivs. I [R = (CH2)2NH(CH2)2Ph, (CH2)2NH(CH2)2Me, (CH2)2NHCH2R1; R1 = 2-, 3-pyridinyl] were synthesized starting form 10.xi.-dihydroartemisinin (II). The synthetic sequence comprised allylation of II with H2C:CHCH2SiMe3 using SnI4 in CH2Cl2, epoxidn. of the allyl side chain of I (R = allyl) using m-CPBA in CH2Cl2, oxidative cleavage of the epoxide to the diol using TFA in CH2Cl2 followed by treatment with NaHCO3 in MeOH, oxidn. of the diol II [R = CH2CH(OH)CH2OH] with NaIO4 to form aldehyde I (R = CH2CHO), and finally, an imidation/redn. of the aldehyde with the corresponding amine using Na2SO4 in CH2Cl2 then treatment with NaBH4 in MeOH.

IT **194409-61-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of nitrogen contg. 12-deoxoartemisinin amine derivs.)

RN 194409-61-5 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(oxiranylmethyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

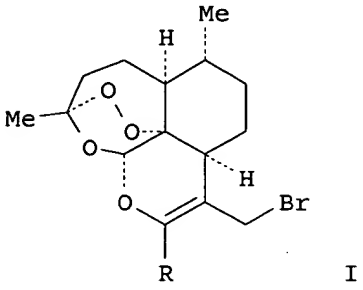
Absolute stereochemistry.



L4 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:769186 CAPLUS
DOCUMENT NUMBER: 138:24842
TITLE: Allylic bromination of anhydrodihydroartemisinin and of its 10-trifluoromethyl analogue: a new access to 16-substituted artemisinin derivatives

09743827

AUTHOR(S): Grellepois, Fabienne; Chorki, Fatima; Ourevitch, Michele; Crousse, Benoit; Bonnet-Delpon, Daniele; Begue, Jean-Pierre
CORPORATE SOURCE: Faculte de Pharmacie, CNRS, BIOCIS, Chatenay-Malabry, F-92296, Fr.
SOURCE: Tetrahedron Letters (2002), 43(43), 7837-7840
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:24842
GI



I

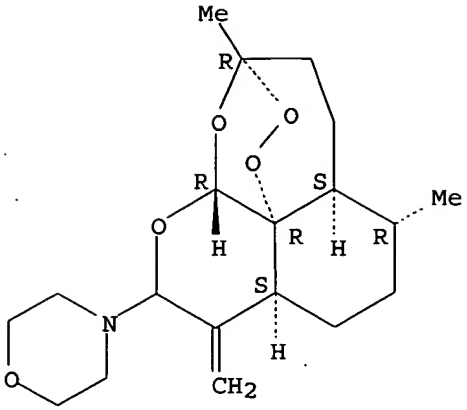
AB The reactivity of the anhydrodihydroartemisinin and of its 10-trifluoromethyl analog toward brominating reagents was explored with the aim of prepg. the new corresponding C-16 allylic bromides I (R = H, CF3). Both glycals react with NBS to provide compds. I (R = H, CF3). From the 10-CF3 anhydrodihydroartemisinin, the allylic bromination also occurred in high yield with Br2 in CCl4. Products I (R = H, CF3) react with N-, O- and C-nucleophiles. From I (R = H), products of SN and SN' were obtained in low to moderate yield, while the CF3-substituted allylic bromide I (R = CF3) only underwent nucleophilic substitution. New fluorinated 16-substituted artemisinin derivs. could be obtained in high yield.

IT **478159-30-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(allylic bromination of anhydrodihydroartemisinin and of its 10-trifluoromethyl analog using NBS or Br2 and subsequent nucleophilic substitution reactions to give fluorinated 16-substituted artemisinin derivs.)

RN 478159-30-7 CAPLUS

CN Morpholine, 4-[(3R,5aS,6R,8aS,12R,12aR)-decahydro-3,6-dimethyl-9-methylene-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

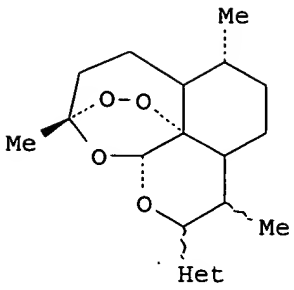


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

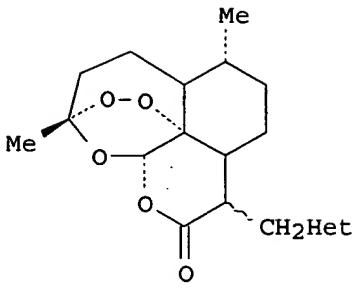
L4 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:105791 CAPLUS
DOCUMENT NUMBER: 136:118602
TITLE: Preparation of arteannuin derivatives containing azacyclic radical
INVENTOR(S): Li, Ying; Liao, Xibin
PATENT ASSIGNEE(S): Shanghai Inst. of Pharmaceutics, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 15 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1296009	A	20010523	CN 1999-124012	19991112
CN 1105722	B	20030416		

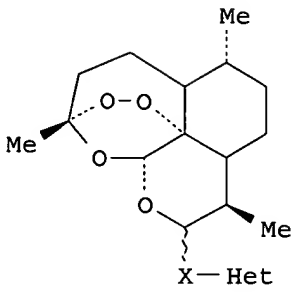
PRIORITY APPLN. INFO.: CN 1999-124012 19991112
OTHER SOURCE(S): CASREACT 136:118602; MARPAT 136:118602
GI



I



II



III

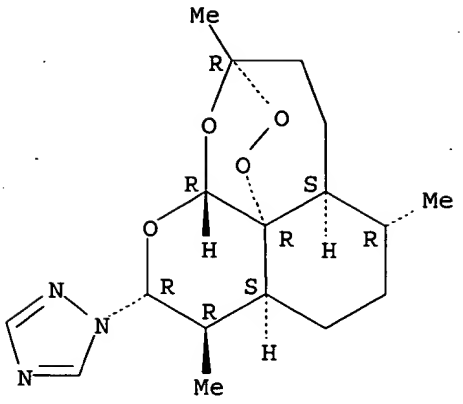
AB Compds. I, II, III (Het = triazole, benzotriazole, benzimidazole, indole, or their derivs. substituted by carboxyl, ester group, acyl, alkoxy, C1-3 alkyl, hydroxy, or hydroxymethyl; X = -OCO-, -OCH2-, -OCH2CH2-, -OCH2CH(OH)CH2-) are claimed. Title compd. were synthesized by the condensation of either acetyldihydroarteannuin or (trichloroacetyl)dihydroarteannuin or methylenearteannuin or dihydroarteannuin or arteannuin 2-bromoethyl ether or arteannuin 2,3-epoxypropyl ether with nitrogen heterocyclic compd. in the presence of acidic catalyst or alk. compds or DCC, giving product with 12% to 61% yield. Thus, dihydroarteannuin dissolved in methylenechloride, adding trifluoroacetic acid anhydrate, reacted under 0-5.degree., forming dihydroarteannuin trifluoroacetate, adding 1,2,4-triazole, using the TLC follow the reaction, after the workup, giving the triazole substituted dihydroarteannuin, with yield 12-20%. Title compds. are of antimalarial, antitumor, immunoregulatory, and anti-inflammatory activity.

IT **390800-25-6P 390800-26-7P 390800-31-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn of arteannuin deriv. contg. azacyclic group)

RN 390800-25-6 CAPLUS

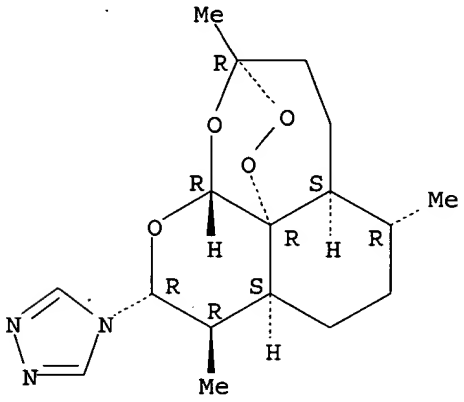
CN 1H-1,2,4-Triazole, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



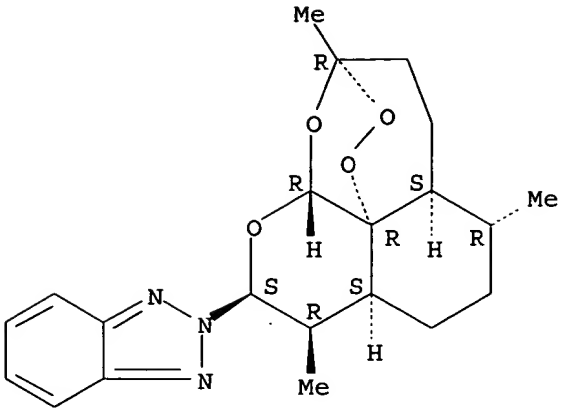
RN 390800-26-7 CAPLUS
CN 4H-1,2,4-Triazole, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



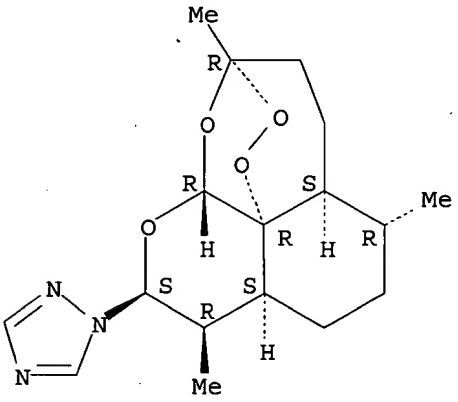
RN 390800-31-4 CAPLUS
CN 2H-Benzotriazole, 2-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



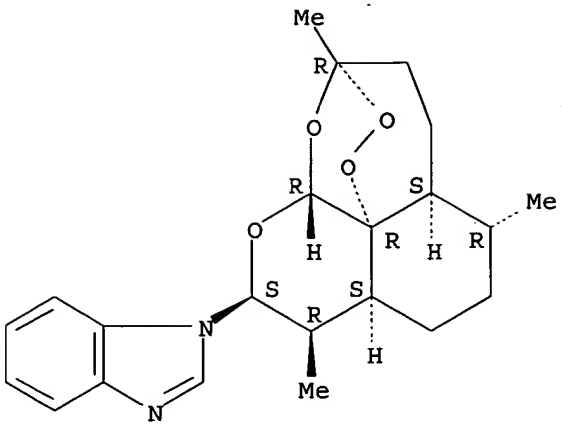
IT **390800-24-5P 390800-27-8P 390800-28-9P**
390800-29-0P 390800-30-3P 390800-32-5P
390800-33-6P 390800-34-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn of arteannuin deriv. contg. azacyclic group)
RN 390800-24-5 CAPLUS
CN 1H-1,2,4-Triazole, 1-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



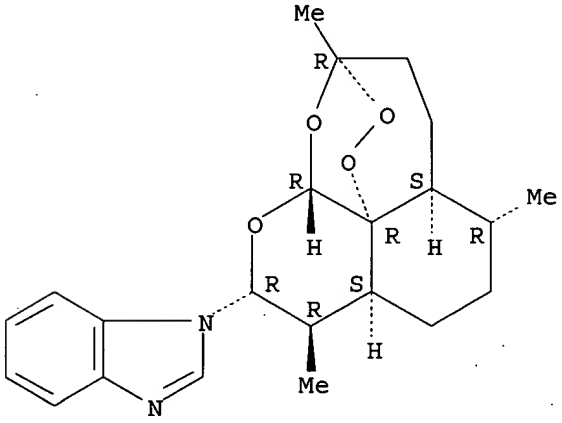
RN 390800-27-8 CAPLUS
CN 1H-Benzimidazole, 1-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



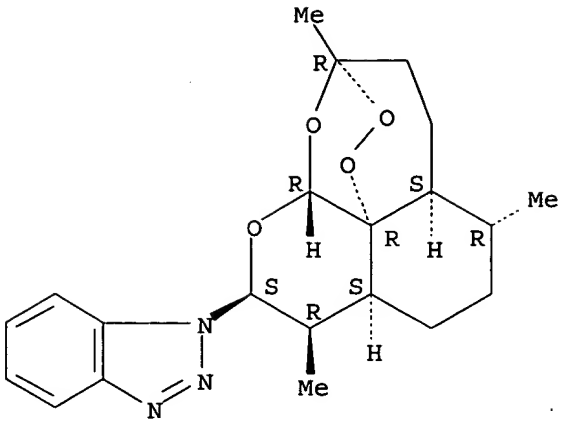
RN 390800-28-9 CAPLUS
CN 1H-Benzimidazole, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



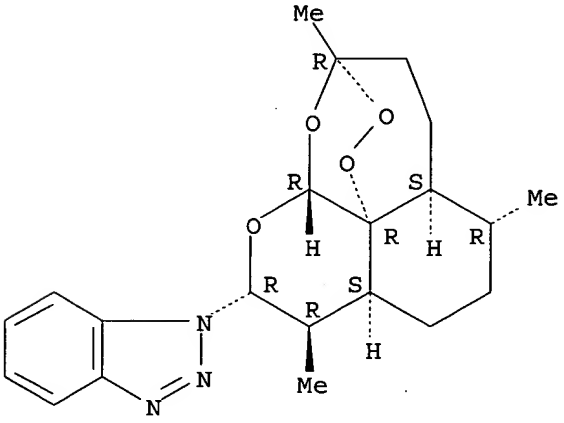
RN 390800-29-0 CAPLUS
CN 1H-Benzotriazole, 1-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



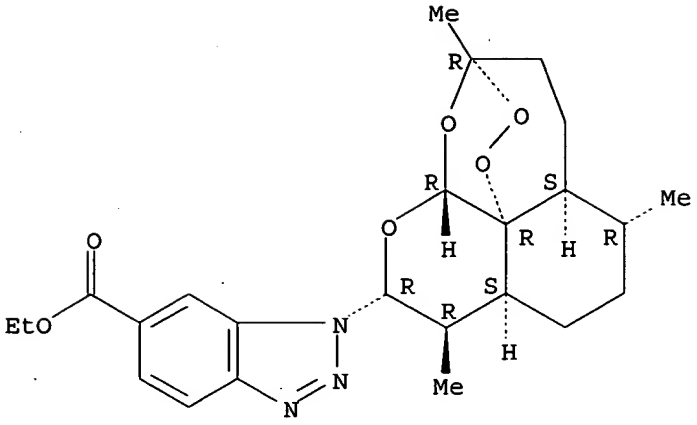
RN 390800-30-3 CAPLUS
CN 1H-Benzotriazole, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



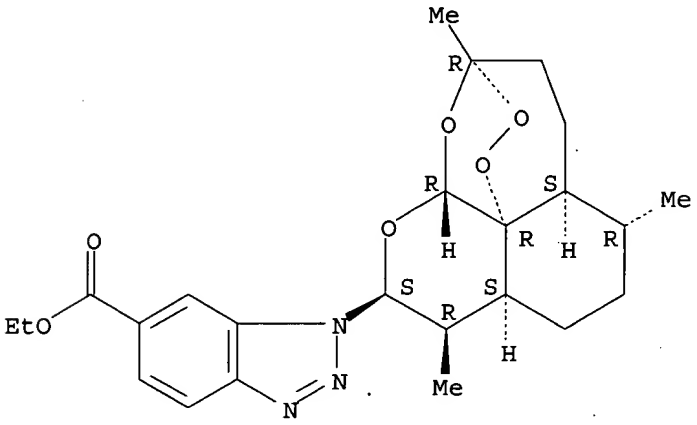
RN 390800-32-5 CAPLUS
CN 1H-Benzotriazole-6-carboxylic acid, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



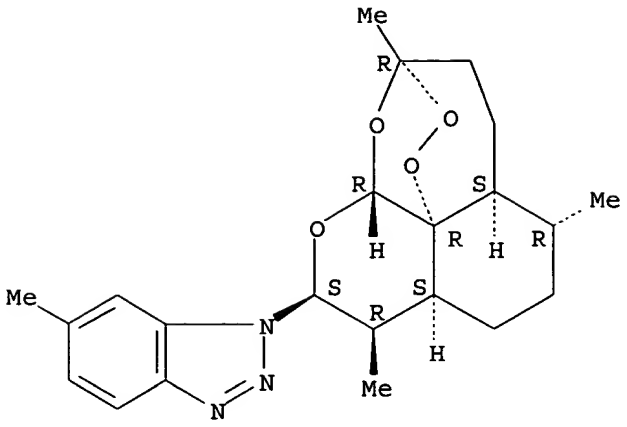
RN 390800-33-6 CAPLUS
CN 1H-Benzotriazole-6-carboxylic acid, 1-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

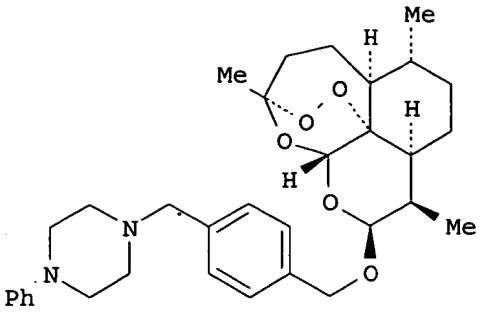


RN 390800-34-7 CAPLUS
CN 1H-Benzotriazole, 1-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-6-methyl-(9CI) (CA INDEX NAME)

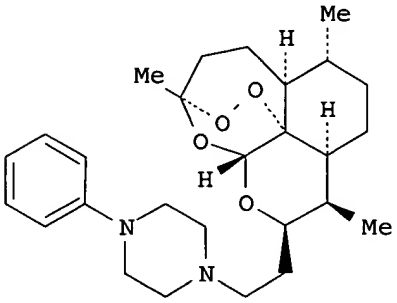
Absolute stereochemistry.



L4 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:96146 CAPLUS
DOCUMENT NUMBER: 136:279571
TITLE: Mechanism-Based Design of Parasite-Targeted Artemisinin Derivatives: Synthesis and Antimalarial Activity of New Diamine Containing Analogues
AUTHOR(S): Hindley, Stephen; Ward, Stephen A.; Storr, Richard C.; Searle, Natalie L.; Bray, Patrick G.; Park, B. Kevin; Davies, Jill; O'Neill, Paul M.
CORPORATE SOURCE: Department of Chemistry, The Robert Robinson Laboratories, University of Liverpool, Liverpool, L69 7ZD, UK
SOURCE: Journal of Medicinal Chemistry (2002), 45(5), 1052-1063
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:279571
GI



I



II

AB The potent antimalarial activity of chloroquine against chloroquine-sensitive strains can be attributed, in part, to its high accumulation in the acidic environment of the heme-rich parasite food vacuole. A key component of this intraparasitic chloroquine accumulation mechanism is a weak base "ion-trapping" effect whereupon the basic drug is concd. in the acidic food vacuole in its membrane-impermeable diprotonated form. By the incorporation of amino functionality into target artemisinin analogs, we hoped to prep. a new series of analogs that, by virtue of increased accumulation into the ferrous-rich vacuole, would display enhanced antimalarial potency. The initial part of the project focused on the prepn. of piperazine-linked analogs, e.g. I. Antimalarial evaluation of these derivs. demonstrated potent activity vs. both chloroquine-sensitive and chloroquine-resistant parasites. On the basis of these observations, we then set about prepg. a series of C-10 carba-linked amino derivs. Optimization of the key synthetic step using a newly developed coupling protocol provided a key intermediate, 10.beta.-allyldeoxoartemisinin in 90% yield. Further elaboration, in three steps, provided nine target C-10 carba analogs, e.g. II in good overall yields. Antimalarial assessment demonstrated that these compds. were 4-fold more potent than artemisinin and about twice as active as artemether in vitro vs. chloroquine-resistant parasites. On the basis of the products obtained from biomimetic Fe(II) degrdn. of the C-10 carba analog II, it was proposed that these analogs may have a mode of action subtly different from that of the parent drug artemisinin and other C-10 ether derivs. such as artemether. Preliminary in vivo testing by the WHO demonstrated that four of these compds. are active orally at doses of less than 10 mg/kg. Since these analogs are available as water-sol. salts and cannot form dihydroartemisinin by P 450-catalyzed oxidn., they represent useful leads that might prove to be superior to the currently used derivs., artemether and artesunate.

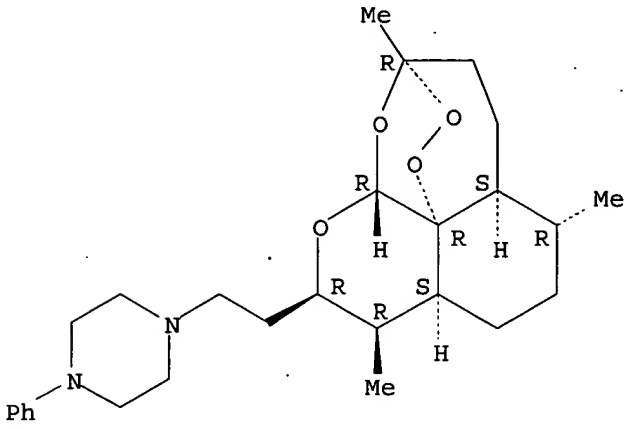
IT **406225-74-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant

or reagent)
(synthesis and antimalarial activity of new artemisinin analogs contg. a diamine moiety)

RN 406225-74-9 CAPLUS

CN Piperazine, 1-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

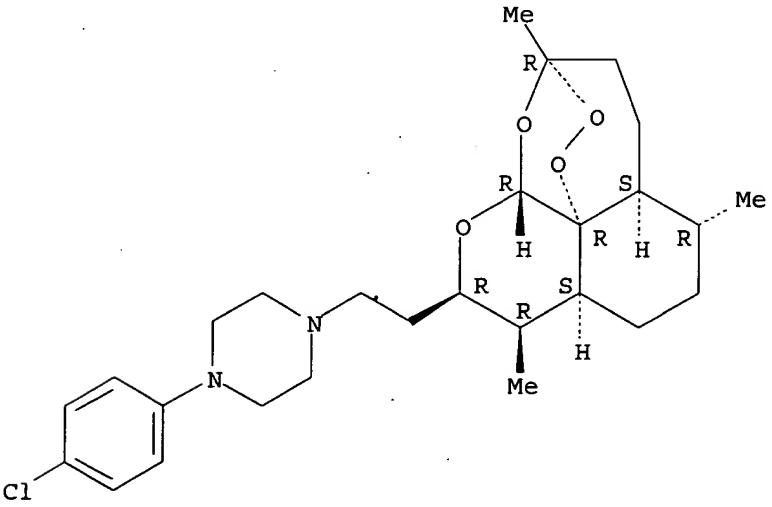


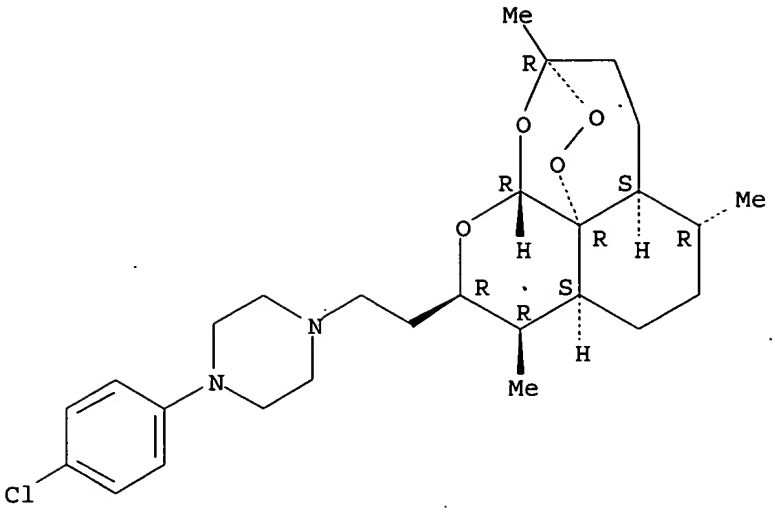
IT **406225-72-7P 406225-73-8P 406225-75-0P 406225-76-1P 406225-77-2P 406225-78-3P 406225-79-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antimalarial activity of new artemisinin analogs contg. a diamine moiety)

RN 406225-72-7 CAPLUS

CN Piperazine, 1-(4-chlorophenyl)-4-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]- (9CI) (CA INDEX NAME)

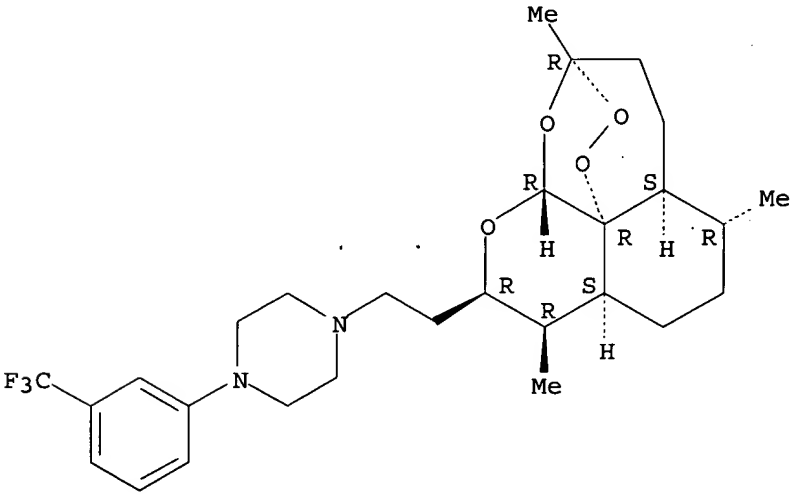
Absolute stereochemistry.





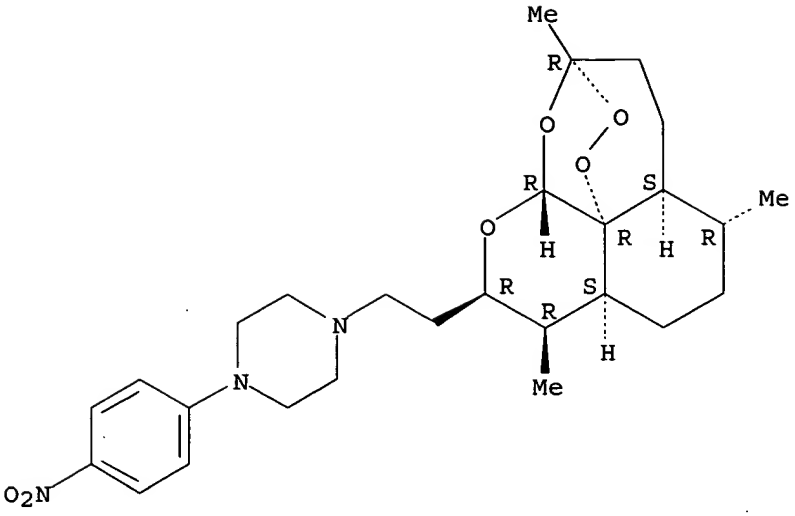
RN 406225-73-8 CAPLUS
CN Piperazine, 1-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



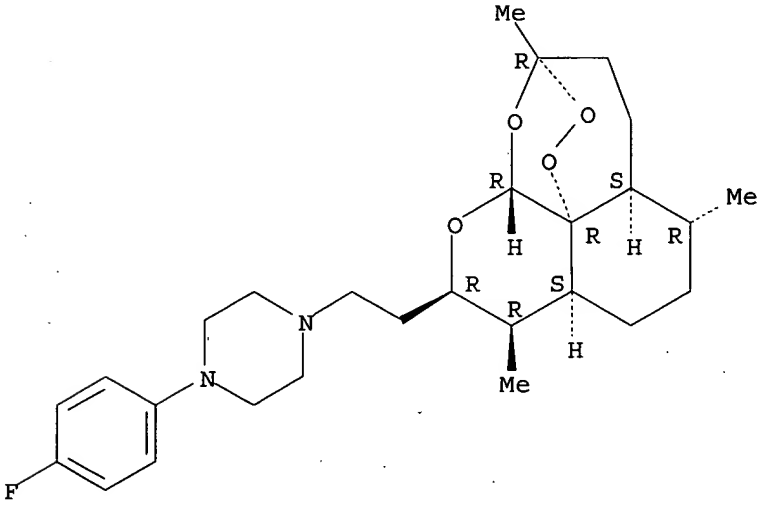
RN 406225-75-0 CAPLUS
CN Piperazine, 1-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]-4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



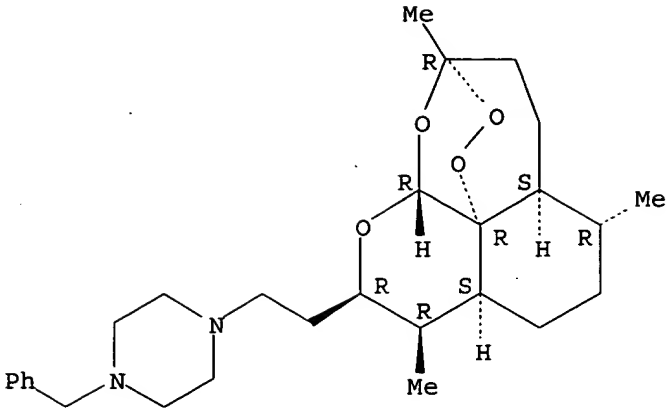
RN 406225-76-1 CAPLUS
CN Piperazine, 1-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]-4-(4-fluorophenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



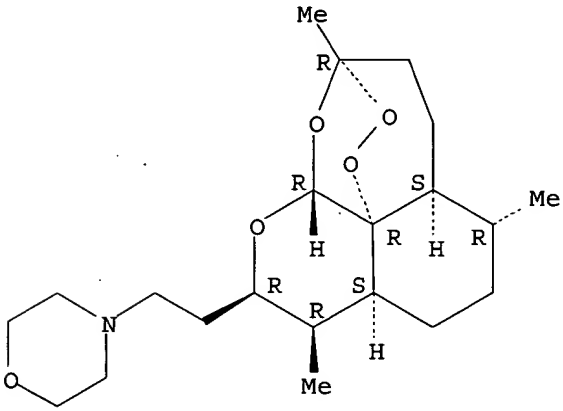
RN 406225-77-2 CAPLUS
CN Piperazine, 1-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



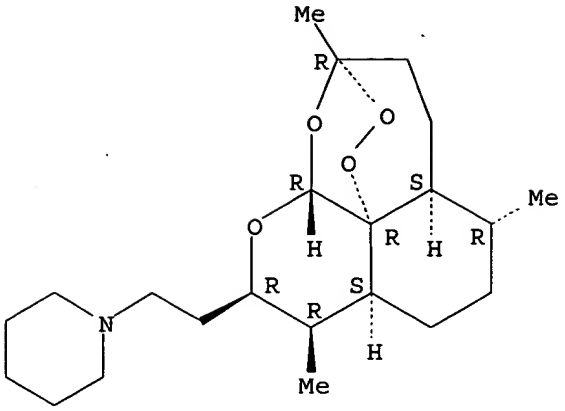
RN 406225-78-3 CAPLUS
CN Morpholine, 4-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 406225-79-4 CAPLUS
CN Piperidine, 1-[2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



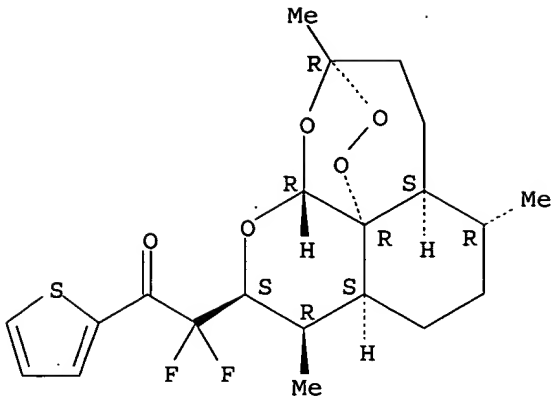
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:745130 CAPLUS
DOCUMENT NUMBER: 136:37784
TITLE: Fluoro Artemisinins: Difluoromethylene Ketones
AUTHOR(S): Chorki, Fatima; Grellepois, Fabienne; Crousse, Benoit; Ourevitch, Michele; Bonnet-Delpon, Daniele; Begue, Jean-Pierre
CORPORATE SOURCE: Faculte de Pharmacie, BIOCIS CNRS, Chatenay-Malabry, F-92296, Fr.
SOURCE: Journal of Organic Chemistry (2001), 66(23), 7858-7863
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:37784

AB The reactions of the ring-contracted aldehydes, derived from anhydrodihydroartemisinin, with gem-difluoroenoxysilanes in the presence of BF3.cntdot.Et2O afforded the corresponding difluoromethylene ketol adducts in good yields. Similar Lewis acid catalyzed reactions of dihydroartemisinin acetate with the difluoroenoxysilanes provided the 10-substituted difluoromethylene ketones in good to moderate yields. Interestingly enough, the course and the stereochem. of these reactions are highly dependent on the nature of the Lewis acids used; the addn. reaction was accompanied by epimerization at C-9, and the stereochem. at C-10 depends on the difluoroenoxysilane used. The best results were obtained using SnCl4 to give the 9.alpha.,10.beta.-stereoisomer in high stereoselectivity. When 0.4 equiv of SnCl4 was used for the reaction with the .alpha.-(4-methoxyphenylenoxysilane)-.beta.,.beta.-difluoroenoxysilane, however, a rearrangement of the endoperoxide was obsd.

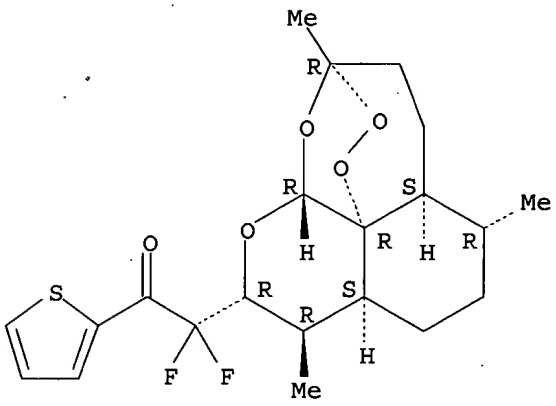
IT **380225-28-5P 380225-38-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of difluoro artemisinins)
RN 380225-28-5 CAPLUS
CN Ethanone, 2-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2,2-difluoro-1-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380225-38-7 CAPLUS
CN Ethanone, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2,2-difluoro-1-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:118528 CAPLUS
DOCUMENT NUMBER: 134:295956
TITLE: C-10-Fluorinated derivatives of dihydroartemisinin: difluoromethylene ketones
AUTHOR(S): Chorki, F.; Crousse, B.; Bonnet-Delpon, D.; Begue, J.-P.; Brigaud, T.; Portella, C.
CORPORATE SOURCE: Faculte de Pharmacie, CNRS, BIOCIS, Chatenay-Malabry, F-92296, Fr.
SOURCE: Tetrahedron Letters (2001), 42(8), 1487-1489
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:295956
AB Difluoroenoxysilanes, prepd. from arom. and heterocyclic ketones, reacted

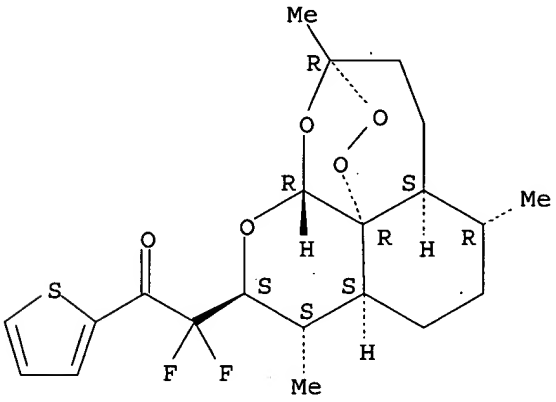
with dihydroartemisinin acetate in the presence of Lewis acid to provide in good to moderate yields the 10-substituted difluoromethylene ketones. The introduction of the difluoromethylketone moiety was accompanied by the epimerization of C9. Best results were obtained using SnCl4 as Lewis acid.

IT **334528-83-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of C10-fluorinated derivs. of dihydroartemisinin from difluoroenoxysilanes)

RN 334528-83-5 CAPLUS

CN Ethanone, 2-[(3R,5aS,6R,8aS,9S,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2,2-difluoro-1-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:874203 CAPLUS
DOCUMENT NUMBER: 134:29575
TITLE: C-10 carbon-substituted artemisinin-like trioxane compounds having antimalarial, antiproliferative and antitumor activities
INVENTOR(S): Posner, Gary H.; Woo, Soon Hyung; Ploypradith, Poonsakdi; Parker, Michael H.; Shapiro, Theresa A.; Elias, Jeffrey S.; Northrop, John; Zheng, Qun Y.; Murray, Christopher; Daughenbaugh, Randall J.
PATENT ASSIGNEE(S): Hauser, Inc., USA; Johns Hopkins University
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 1,242.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6160004	A	20001212	US 1998-183693	19981030
US 6156790	A	20001205	US 1997-1242	19971230
CA 2317112	AA	19990708	CA 1998-2317112	19981230
WO 9933461	A1	19990708	WO 1998-US27717	19981230

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9920184	A1	19990719	AU 1999-20184	19981230
AU 739687	B2	20011018		
EP 1043988	A1	20001018	EP 1998-964977	19981230
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001527043	T2	20011225	JP 2000-526218	19981230

PRIORITY APPLN. INFO.:
US 1997-1242 A2 19971230
US 1998-183693 A 19981030
WO 1998-US27717 W 19981230

OTHER SOURCE(S): MARPAT 134:29575
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

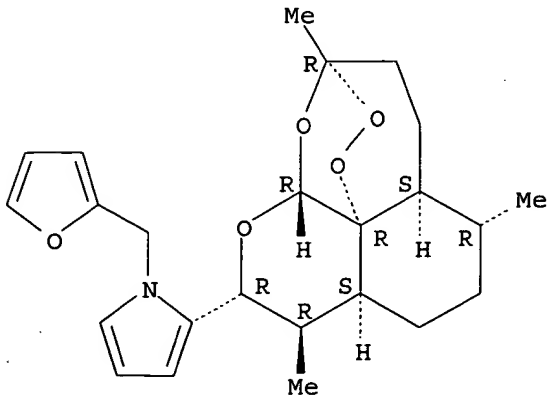
AB This invention provides a two-step procedure for the replacement of the pyranose anomeric 10-OH group in dihydroartemisinin by a variety of carbon nucleophiles, resulting in the prepn. of C-10 carbon-substituted compds. [I; x = 1, 2, 3; R = (un)substituted aryl, heteroaryl, alkenyl, alkyl, polyethylene glycol, aroylmethylene, alkanoylmethylene, alkenyl, diketone, bis-acetylene, etc.] as antimalarial, antiproliferative and antitumor agents. Thus, .beta.-artemether (II) reacted with 1,4-bis[1-(trimethylsilyloxy)vinyl]benzene (also prepd.) in CH2Cl2 contg. 1M soln. of TiCl4 at -78.degree. for 1 h to give 13% (III), whose antimalarial activity was ca. 5 times that of artemisinin.

IT **220115-01-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antimalarial, antiproliferative and antitumor C-10 carbon-substituted artemisinin-like trioxane compds.)

RN 220115-01-5 CAPLUS

CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(2-furanylmethyl)-(9CI) (CA INDEX NAME)

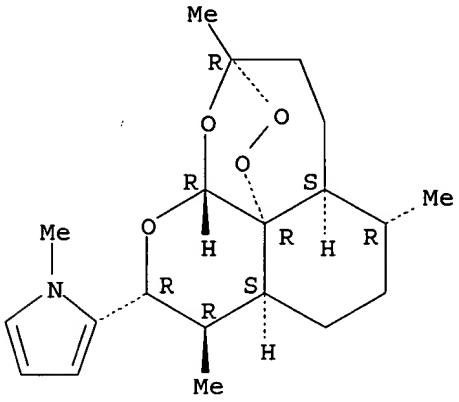
Absolute stereochemistry. Rotation (+).



IT **204503-67-3P 204503-68-4P 220115-05-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of antimalarial, antiproliferative and antitumor C-10 carbon-substituted artemisinin-like trioxane compds.)

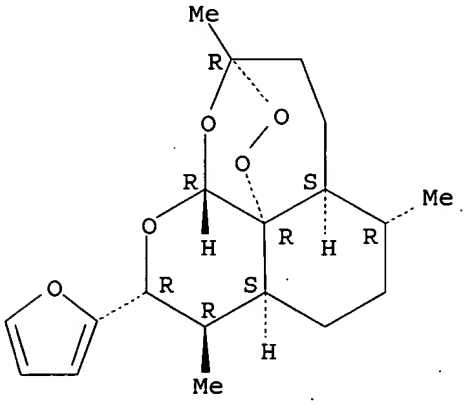
RN 204503-67-3 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



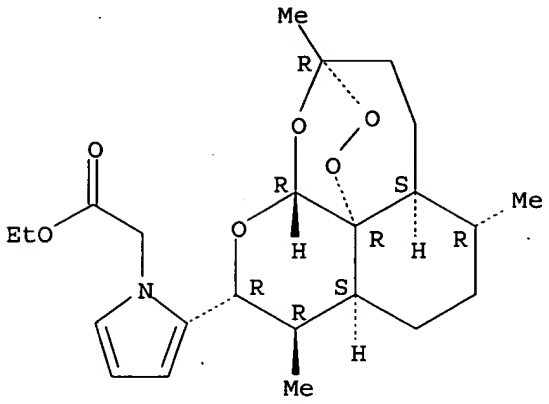
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 220115-05-9 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

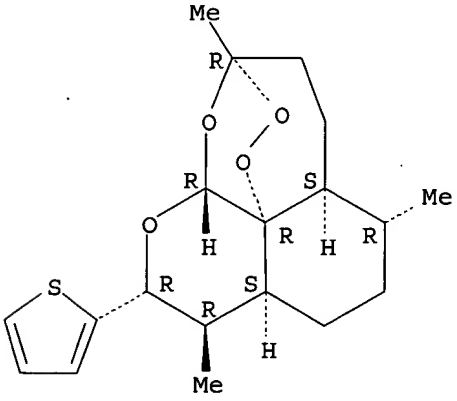


IT **193348-60-6P 220114-93-2P 220114-96-5P**
220114-98-7P 220115-00-4P 220115-04-8P
220115-08-2P 229981-72-0P 229981-88-8P
229981-89-9P 312487-52-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antimalarial, antiproliferative and antitumor C-10 carbon-substituted artemisinin-like trioxane compds.)

RN 193348-60-6 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(2-thienyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

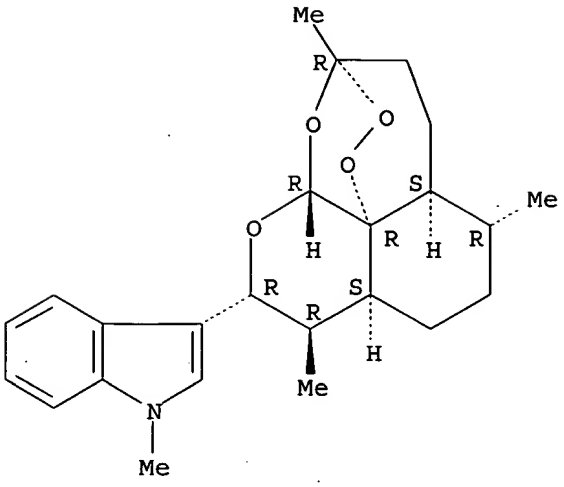
Absolute stereochemistry. Rotation (+).



RN 220114-93-2 CAPLUS

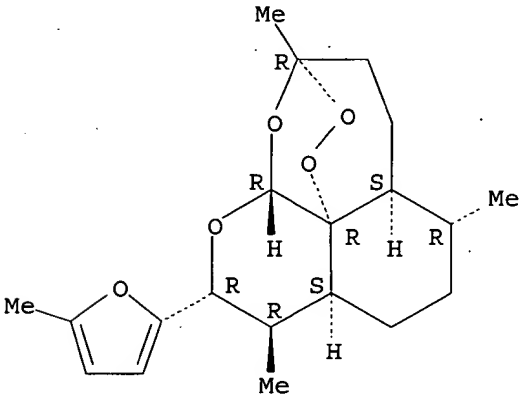
CN 1H-Indole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



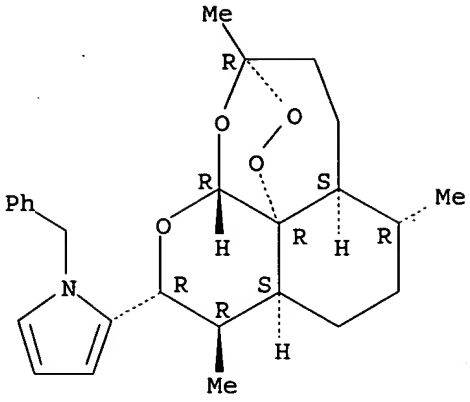
RN 220114-96-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(5-methyl-2-furanyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



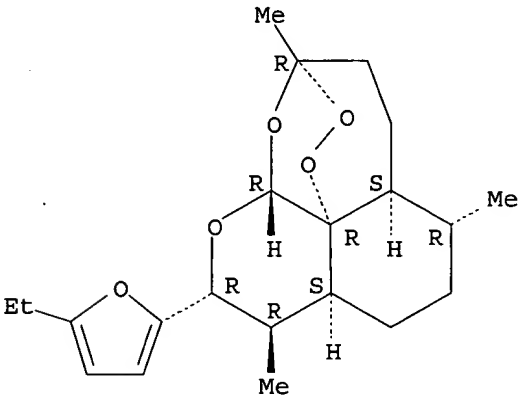
RN 220114-98-7 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



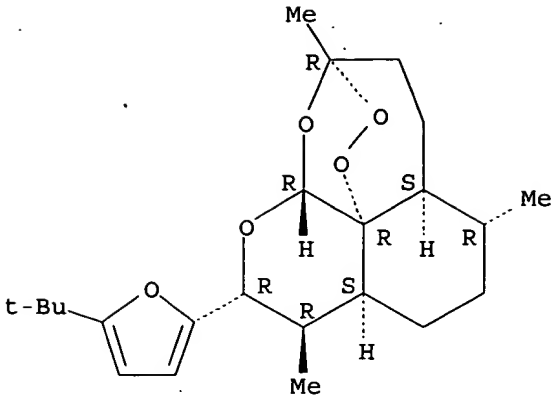
RN 220115-00-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(5-ethyl-2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



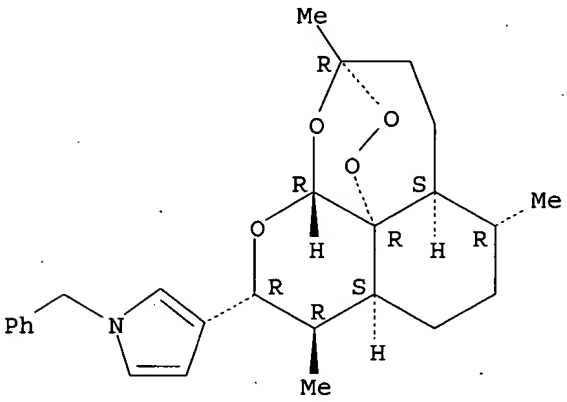
RN 220115-04-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-[5-(1,1-dimethylethyl)-2-furanyl]decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



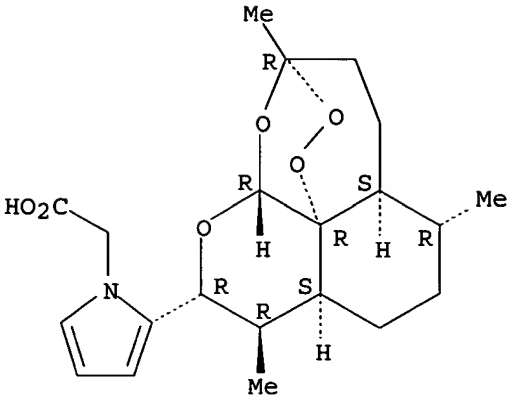
RN 220115-08-2 CAPLUS
CN 1H-Pyrrole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



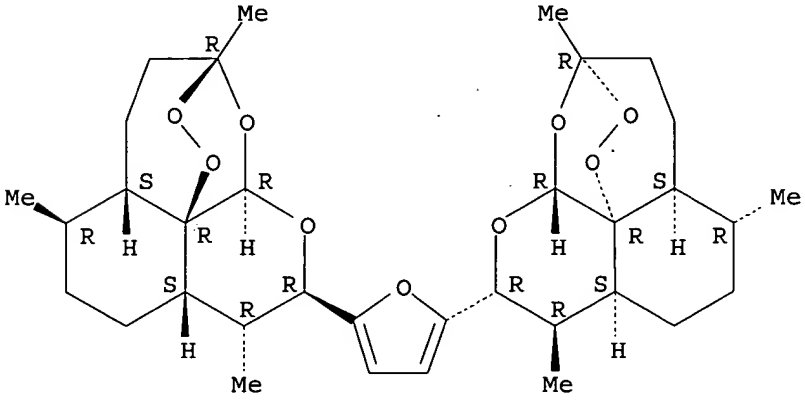
RN 229981-72-0 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



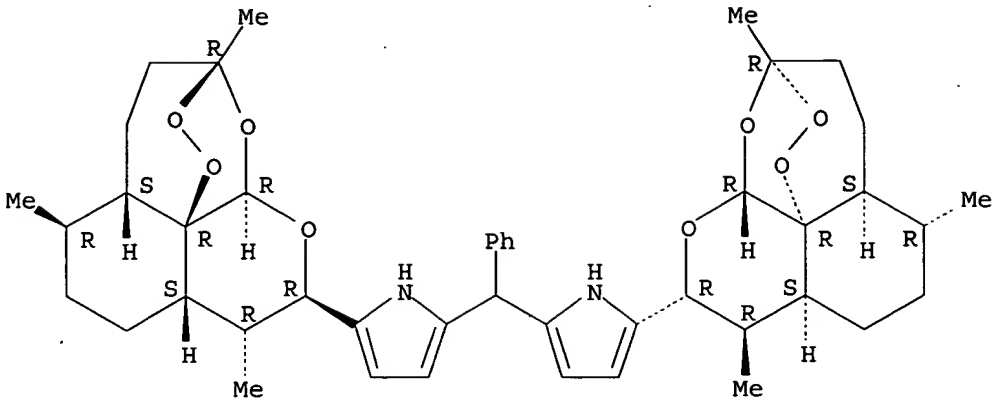
RN 229981-88-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10,10'-(2,5-furandiyl)bis[decahydro-3,6,9-trimethyl-, (3R,3'R,5aS,5'aS,6R,6'R,8aS,8'aS,9R,9'R,10R,10'R,12R,12'R,12aR,12'aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



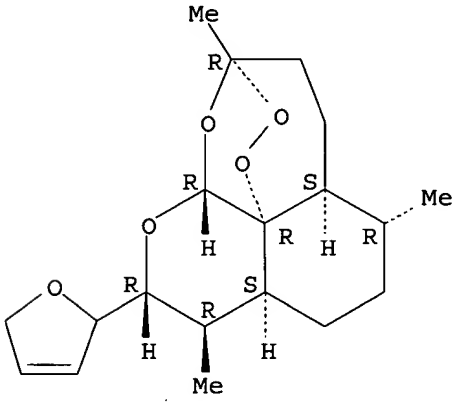
RN 229981-89-9 CAPLUS
CN 1H-Pyrrole, 2,2'-(phenylmethylene)bis[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 312487-52-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2,5-dihydro-2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

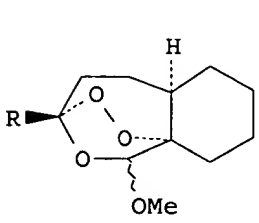


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:754503 CAPLUS
DOCUMENT NUMBER: 133:309909
TITLE: Water-soluble trioxanes as potent and safe antimalarial agents
INVENTOR(S): Posner, Gary H.; Parker, Michael H.; Krasavin, Mikhail; Shapiro, Theresa A.
PATENT ASSIGNEE(S): Johns Hopkins University, USA
SOURCE: U.S., 18 pp., Cont.-in-part of U.S. 5,932,591. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6136847 A 20001024 US 1999-287353 19990407
US 5932591 A 19990803 US 1996-758661 19961202
WO 2000059501 A1 20001012 WO 2000-US9309 20000407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1996-758661 A2 19961202
US 1999-287353 A 19990407
OTHER SOURCE(S): MARPAT 133:309909
GI



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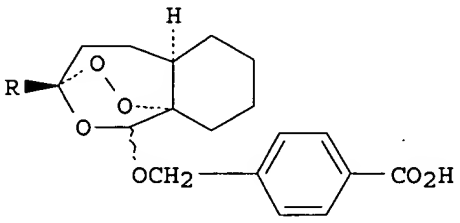
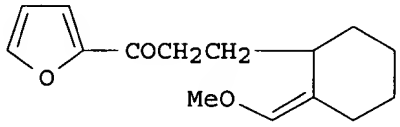


II



III

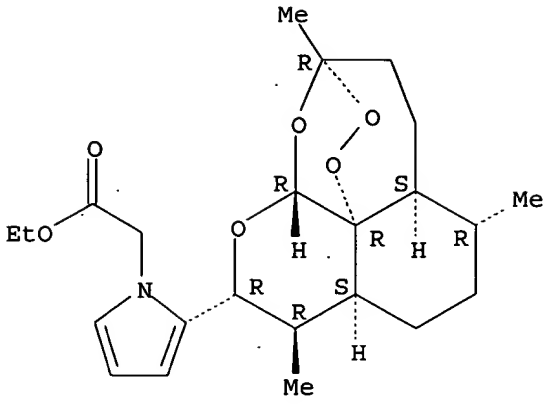
AB Trioxanes such as I [R = (un)substituted aryl, heteroaryl, alkyl] and II [R = (un)substituted alkyl, alkenyl, aryl, heteroaryl] were prepd. as antimalarial agents. Thus, a CH2Cl2 soln. of ketone III and methylene blue was treated with O2 and UV light at -78.degree., tert-butyldimethylsilyl triflate in CH2Cl2 was added, the mixt. was stirred 8 h at -78.degree., and the reaction was quenched by addn. of Et3N to give I (R = 2-furanyl; MeO group .alpha.). In antimalarial tests the trioxane products showed IC50 values of 15 to >2500 nM.

IT **220115-05-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(water-sol. trioxanes as potent and safe antimalarial agents)

RN 220115-05-9 CAPLUS

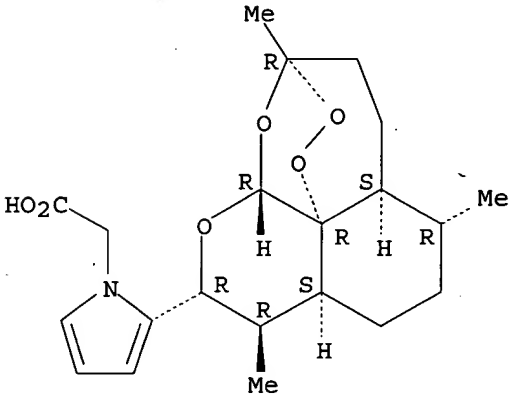
CN 1H-Pyrrole-1-acetic acid, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



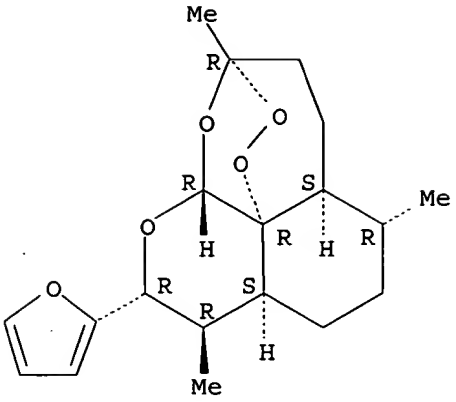
IT **229981-72-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(water-sol. trioxanes as potent and safe antimalarial agents)
RN 229981-72-0 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **204503-68-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(water-sol. trioxanes as potent and safe antimalarial agents)
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

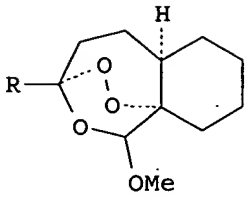


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:725462 CAPLUS
DOCUMENT NUMBER: 133:296575
TITLE: synthesis and activity of water-soluble trioxanes as potent and safe antimalarial agents
INVENTOR(S): Posner, Gary H.; Parker, Michael H.; Krasavin, Mikhail; Shapiro, Theresa A.
PATENT ASSIGNEE(S): Johns Hopkins University, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059501	A1	20001012	WO 2000-US9309	20000407
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6136847	A	20001024	US 1999-287353	19990407

PRIORITY APPLN. INFO.: US 1999-287353 A 19990407
US 1996-758661 A2 19961202
OTHER SOURCE(S): MARPAT 133:296575
GI



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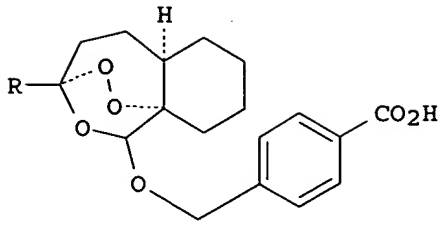


II

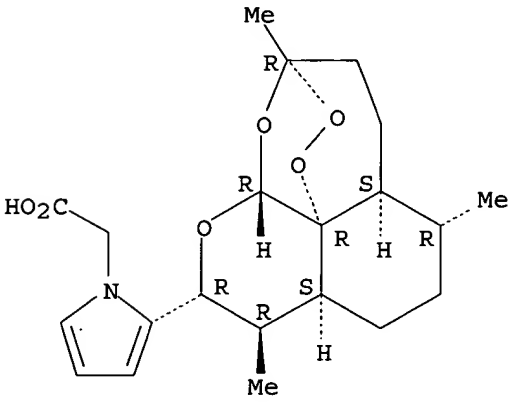
AB Synthesis of biol.-active, water sol., 3-substituted trioxanes (I) [R = substituted aryl, (un)substituted heteroaryl, alkyl] and C12-(p-carboxy)benzyloxy trioxanes (II) [R = (un)substituted alkyl, alkenyl, aryl, heteroaryl] and methods for their use as antiparasitic agents, particularly for the treatment of malaria is disclosed. Thus, I (R = 4-F-C6H4) (III) is prepd. is by arylation of 2-methyoxymethylidenocyclohexanepropanenitrile with 4-fluorophenylmagnesium bromide followed by trioxane formation with singlet oxygen. III shows antimalarial activity at 65 nM.

IT **229981-72-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of water-sol. trioxanes as potent and safe antimalarial agents)

RN 229981-72-0 CAPLUS

CN 1H-Pyrrole-1-acetic acid, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

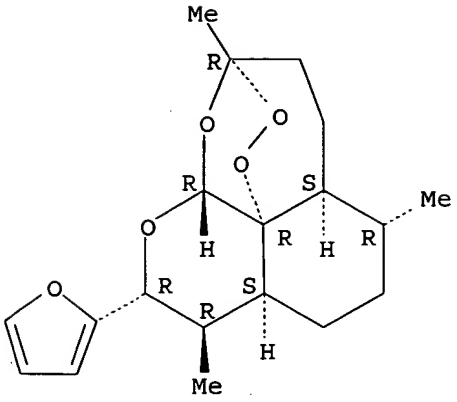


IT **204503-68-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and activity of water-sol. trioxanes as potent and safe antimalarial agents)

RN 204503-68-4 CAPLUS

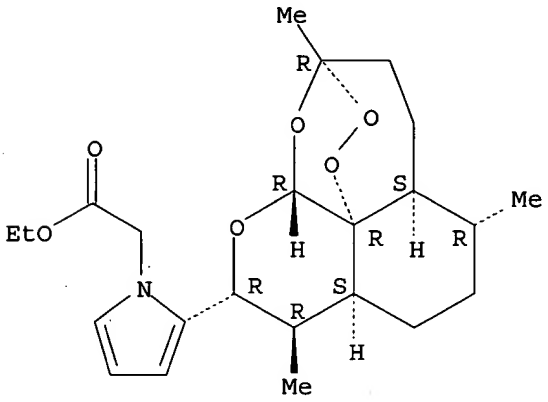
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **220115-05-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and activity of water-sol. trioxanes as potent and safe antimalarial agents)
RN 220115-05-9 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

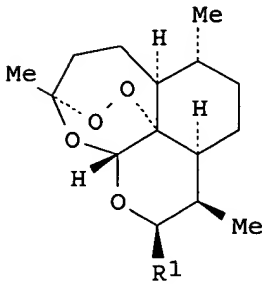
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:667674 CAPLUS
DOCUMENT NUMBER: 134:17600
TITLE: Syntheses and Antimalarial Activities of 10-Substituted Deoxoartemisinins
AUTHOR(S): Ma, Jingyuan; Katz, Esther; Kyle, Dennis E.; Ziffer, Herman
CORPORATE SOURCE: Laboratory of Bioorganic Chemistry and Laboratory of Chemical Physics, NIDDK, Bethesda, MD, 20892-0510, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(22), 4228-4232
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:17600
GI



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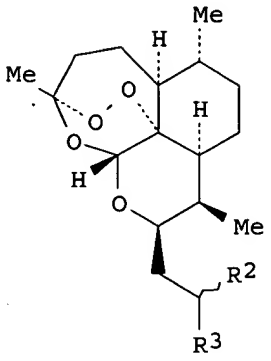


II

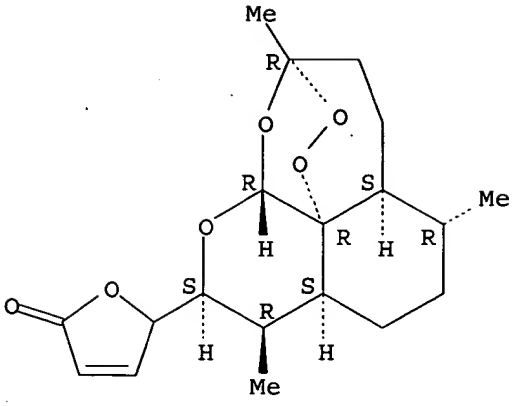
AB Two series of 10-substituted deoxoartemisinin derivs. [(I; R1 = CH2COC(Me)3, CH2CHO, CH2COMe, CH2COPh, 2-oxocyclopentyl, 5-oxo-2,5-dihydrofuran-2-yl, CN) and (II; R2 = .alpha.-OH, .beta.-OH; R3 = Me, Et, CH(Me)2, C(Me)3)] have been synthesized. I employed the reaction of dihydroartemisinin acetate with several silyl enol ethers in the presence of titanium tetrachloride. II utilized the reaction of 10-(2-oxoethyl)deoxoartemisinin with several Grignard reagents. The in vitro antimalarial activities of I and II were detd. against two drug-resistant clones of P. falciparum. The activities of II (R2 = .beta.-OH, R3 = Et) and II (R2 = .beta.-OH, R3 = C(Me)3) were 5-7 times greater than that of artemisinin.

IT **253774-89-9P 307297-18-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(syntheses and antimalarial activities of 10-substituted deoxoartemisinins)

RN 253774-89-9 CAPLUS

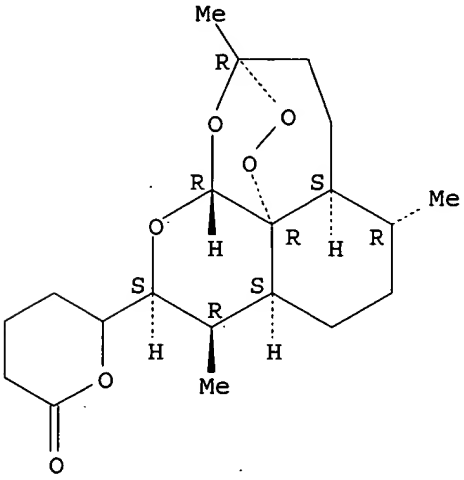
CN 2(5H)-Furanone, 5-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 307297-18-3 CAPLUS
CN 2H-Pyran-2-one, 6-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:646359 CAPLUS
DOCUMENT NUMBER: 133:329129
TITLE: Modeling antimalarial activity: application of kinetic energy density quantum similarity measures as descriptors in QSAR
AUTHOR(S): Girones, Xavier; Gallegos, Ana; Carbo-Dorca, Ramon
CORPORATE SOURCE: Spain
SOURCE: Journal of Chemical Information and Computer Sciences (2000), 40(6), 1400-1407
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

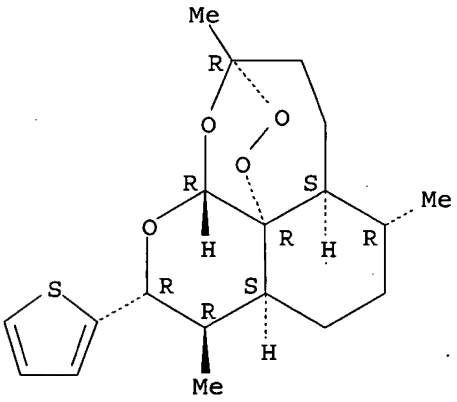
AB In this work, is studied the application, within a quantum similarity framework, of the recently described Kinetic Energy D. Function in the evaluation of the antimalarial activity. First, this new type of D. Function is briefly presented from its theor. foundations, and its inclusion in the mol. quantum similarity is discussed afterward. The application of Kinetic Energy-based Quantum Similarity Measures to QSAR is tested with 2 mol. sets composed of artemisinin derivs., in which the 50% inhibition of synthesis and redn. of hydrofolate (IC50) in different Plasmodium falciparum clones are analyzed. Satisfactory correlations are obtained for all antimalarial activities in all studied mol. sets. Mol. Quantum Similarity anal. provides a consistent, unbiased, and homogeneous set of mol. descriptors and is a feasible alternative to the use of classical physicochem. descriptors.

IT **193348-60-6 204503-67-3 204503-68-4 220114-93-2 220114-96-5 220114-98-7 220115-00-4 220115-01-5 220115-04-8 220115-05-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(modeling antimalarial activity: application of kinetic energy d. quantum similarity measures as descriptors in QSAR)

RN 193348-60-6 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(2-thienyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

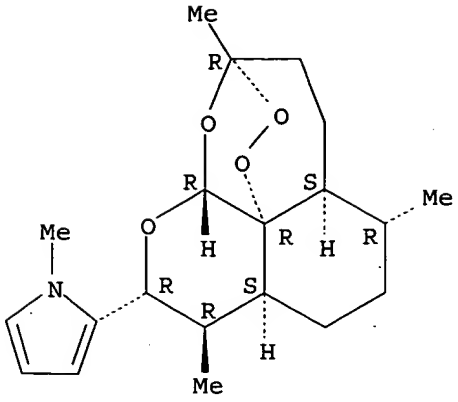
Absolute stereochemistry. Rotation (+).



RN 204503-67-3 CAPLUS

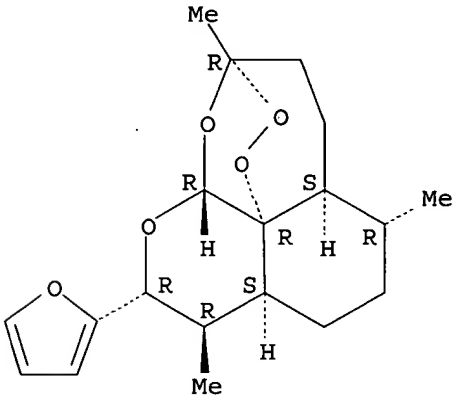
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



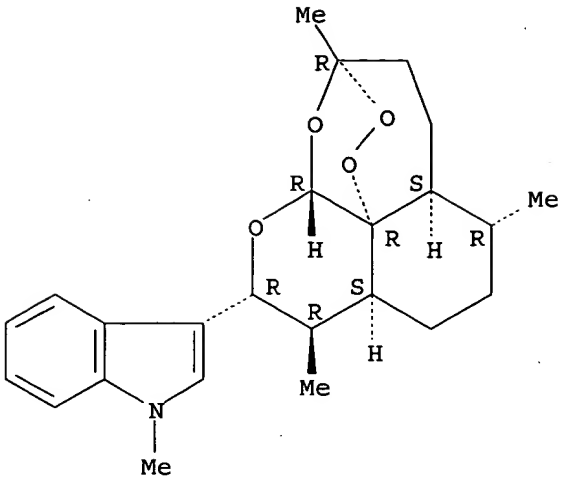
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



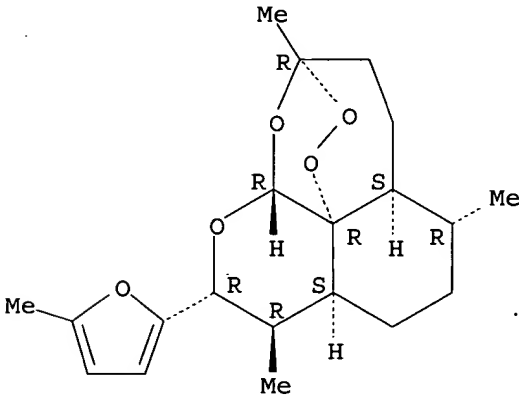
RN 220114-93-2 CAPLUS
CN 1H-Indole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



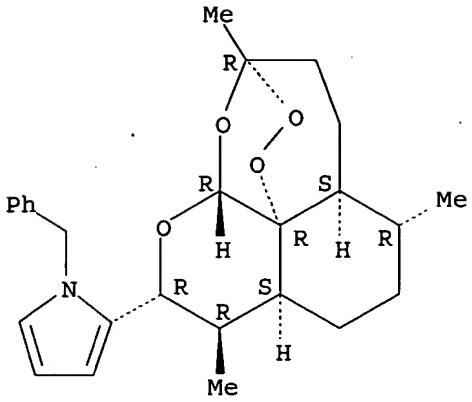
RN 220114-96-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(5-methyl-2-furanyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



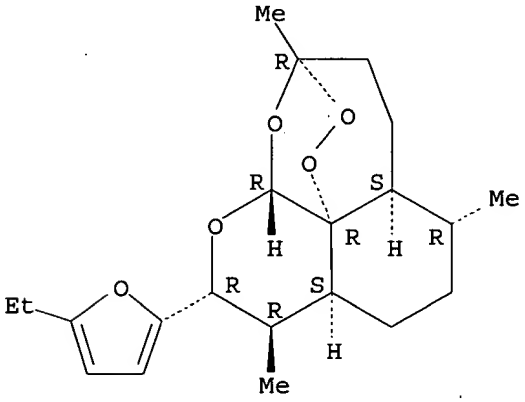
RN 220114-98-7 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



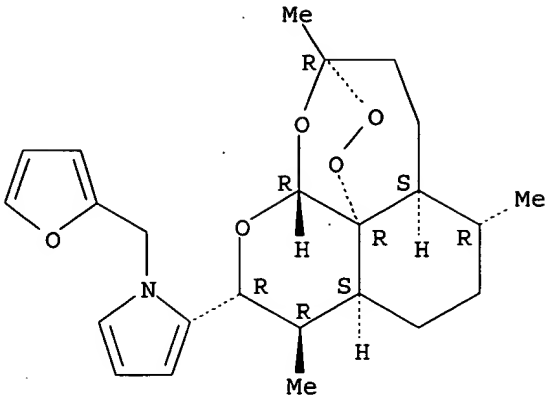
RN 220115-00-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(5-ethyl-2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



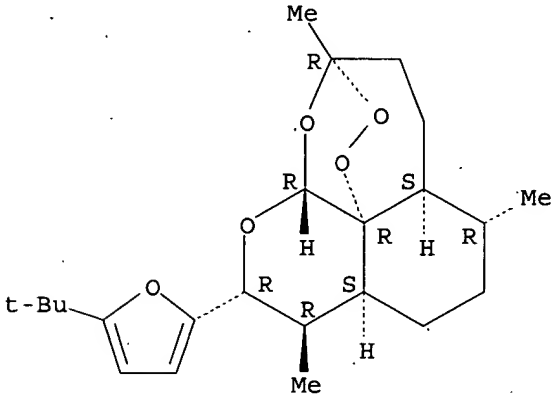
RN 220115-01-5 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(2-furanylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



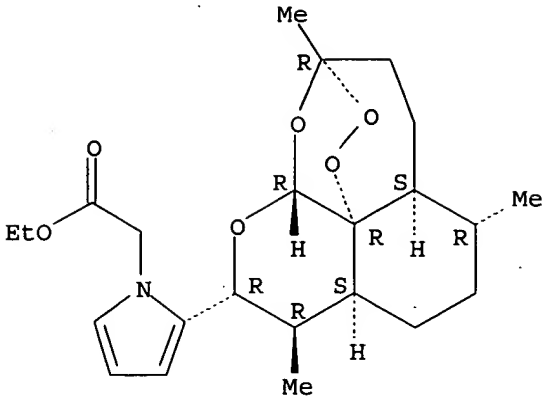
RN 220115-04-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-[5-(1,1-dimethylethyl)-2-furanyl]decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 220115-05-9 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

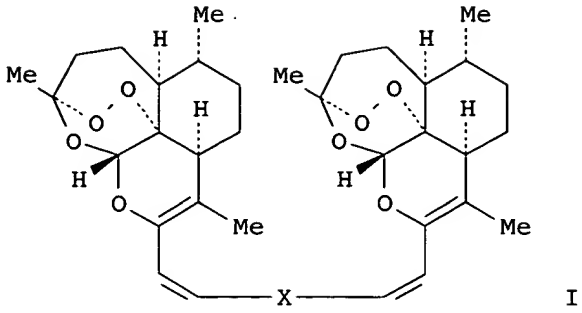


REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:493548 CAPLUS
DOCUMENT NUMBER: 133:89660
TITLE: Preparation of artemisinin analogs having antimalarial, antiproliferative, and antitumor activities
INVENTOR(S): Posner, Gary H.; Murray, Christopher; O'Dowd, Hardwin; Xie, Suji; Shapiro, Theresa A.
PATENT ASSIGNEE(S): Hauser, Inc., USA; Johns Hopkins University
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042046	A1	20000720	WO 2000-US618	20000111
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6297272	B1	20011002	US 1999-228668	19990112
CA 2360383	AA	20000720	CA 2000-2360383	20000111
EP 1150984	A1	20011107	EP 2000-905584	20000111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002055528	A1	20020509	US 2001-887922	20010622
US 6586464	B2	20030701		

PRIORITY APPLN. INFO.: US 1999-228668 A 19990112
WO 2000-US618 W 20000111
OTHER SOURCE(S): MARPAT 133:89660
GI



I

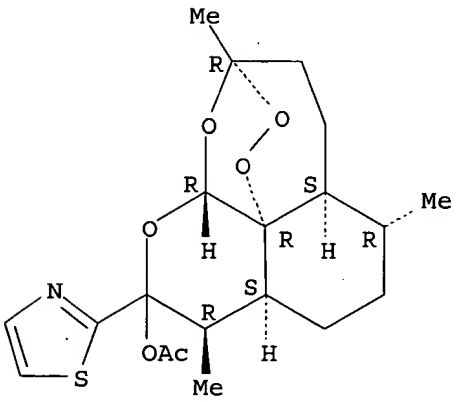
AB Artemisinin analogs, such as dimers I [X = alkylene, heteroalkylene, alkynylene, arylene, heteroarylene], were prepd. for use as antimalarial and antitumor agents. Thus, I (X = 4-C6H4) was prepd. in 63% yield with 3:2:1 EE:EZ:ZZ isomer ratio by a Witting coupling reaction of (3R,5aS,6R,8aS,12R,12aR)-3,4,5,5a,6,7,8,8a-octahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-carboxaldehyde with 1,4-xylylenebis(triphenylphosphonium bromide) using BuLi in THF. The prepd. artemisinin analogs were for antiproliferative activity against a variety of cancer cell lines.

IT **226952-16-5P 226952-32-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of artemisinin analogs having antimalarial, antiproliferative, and antitumor activities)

RN 226952-16-5 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ol, decahydro-3,6,9-trimethyl-10-(2-thiazolyl)-, acetate (ester), (3R,5aS,6R,8aS,9R,12R,12aR)-(9CI) (CA INDEX NAME)

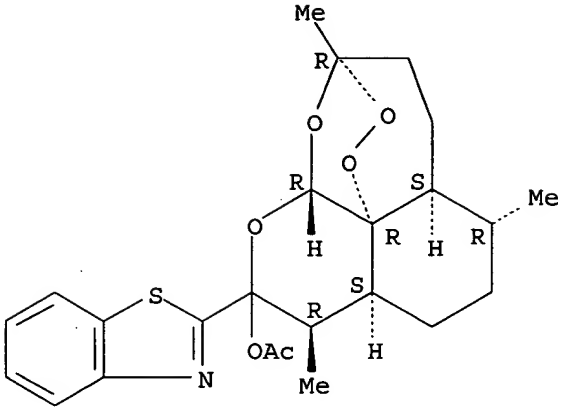
Absolute stereochemistry.



RN 226952-32-5 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ol, 10-(2-benzothiazolyl)decahydro-3,6,9-trimethyl-, acetate (ester), (3R,5aS,6R,8aS,9R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

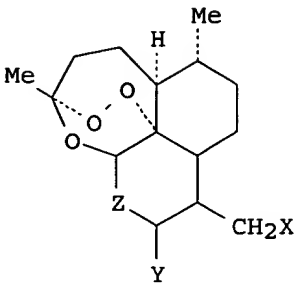


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

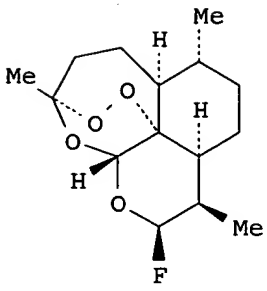
L4 ANSWER 15 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:68461 CAPLUS
DOCUMENT NUMBER: 132:108120
TITLE: Preparation of artemisinin derivatives for use as antitumor agents
INVENTOR(S): Haynes, Richard Kingston; Chan, Ho-Wai; Lam, Wai-Lun; Tsang, Hing-Wo; Hsiao, Wen-Luan
PATENT ASSIGNEE(S): Hong Kong University of Science and Technology, Peop. Rep. China; Wallace, Sheila Jane
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004026	A1	20000127	WO 1999-GB2276	19990714
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9949224	A1	20000207	AU 1999-49224	19990714
EP 1095043	A1	20010502	EP 1999-933049	19990714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1998-305593 A 19980714
EP 1998-308283 A 19981012
WO 1999-GB2276 W 19990714
OTHER SOURCE(S): MARPAT 132:108120
GI



I



II

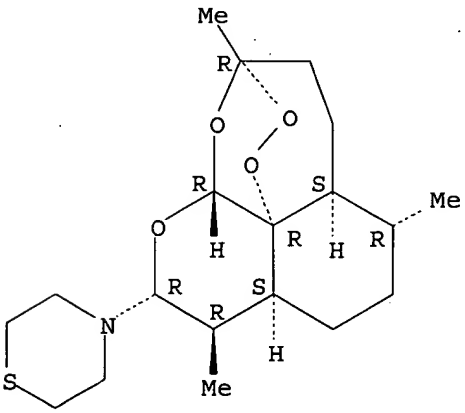
AB Artemisinin derivs. I [X = H, amino, alkyl, aryl; Y = H, OH, oxo, halogen, aryl, cycloalkyl, heteroaryl, amino, acyl, aryloxy, etc.; Z = O, imino], which contg. a trioxane moiety and have cancer cell cytotoxicity, were prepd. for use in the treatment of cancer. Some of these compds. comprise a ligand which is capable of binding to a nucleic acid and a group contg. a trioxane moiety which is capable of acting as source of free radicals which are capable of chem. interacting with a nucleic acid. Thus, II was prepd. in 50.5% yield by fluorination of 10.xi.-dihydroartemisinin using diethylaminosulfur trifluoride (DAST) in CH2Cl2. The prepd. compds. were tested for cytotoxicity against R6 and R6T24 cancer cell lines.

IT **255730-17-7P 255730-31-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of artemisinin derivs. for use as antitumor agents)

RN 255730-17-7 CAPLUS

CN Thiomorpholine, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

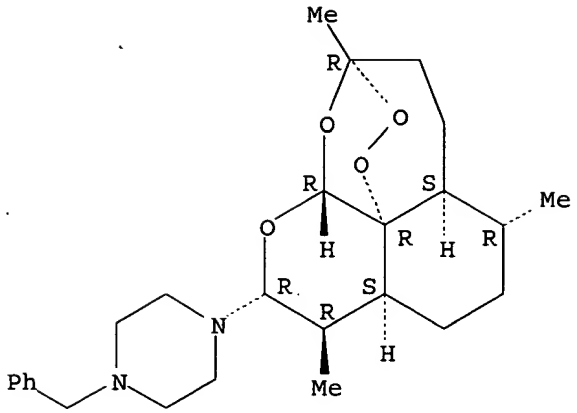
Absolute stereochemistry. Rotation (+).



RN 255730-31-5 CAPLUS

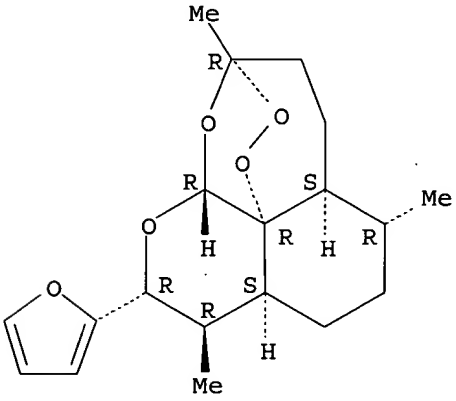
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



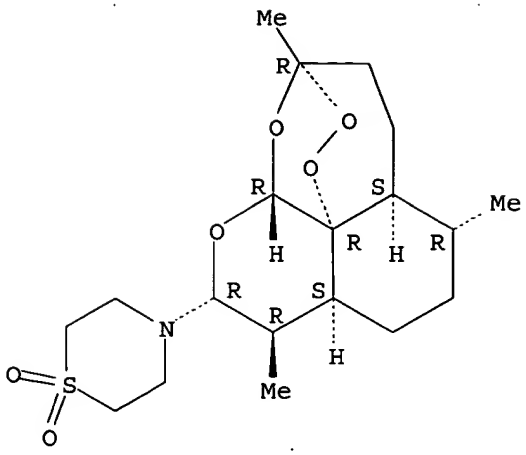
IT **204503-68-4P 255730-18-8P 255730-32-6P**
255730-33-7P 255730-47-3P 255730-49-5P
255730-50-8P 255730-58-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of artemisinin derivs. for use as antitumor agents)
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



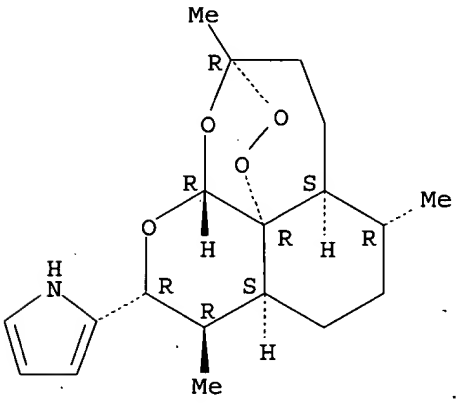
RN 255730-18-8 CAPLUS
CN Thiomorpholine, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



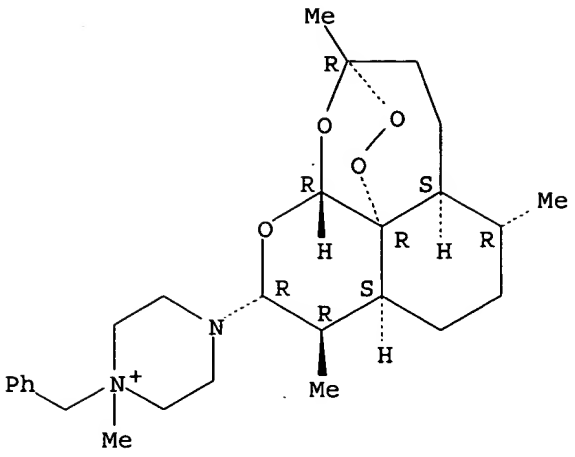
RN 255730-32-6 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 255730-33-7 CAPLUS
CN Piperazinium, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl-1-(phenylmethyl)-, iodide (9CI) (CA INDEX NAME)

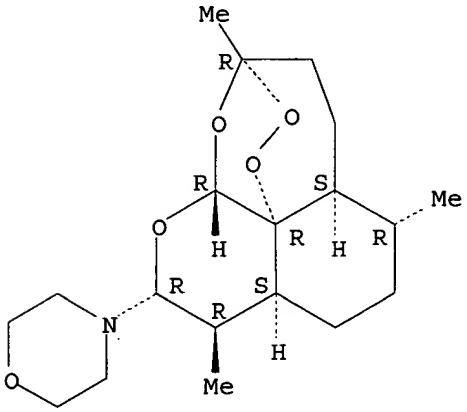
Absolute stereochemistry. Rotation (+).



● I^-

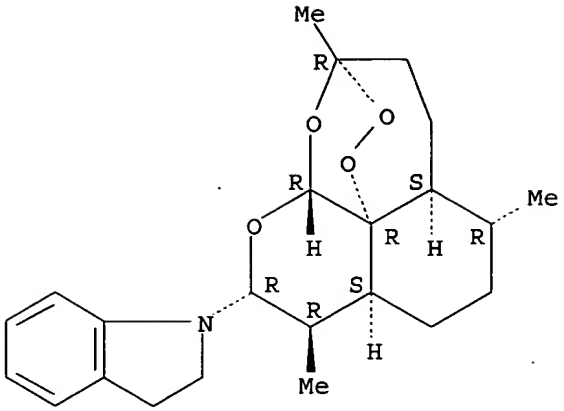
RN 255730-47-3 CAPLUS
CN Morpholine, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



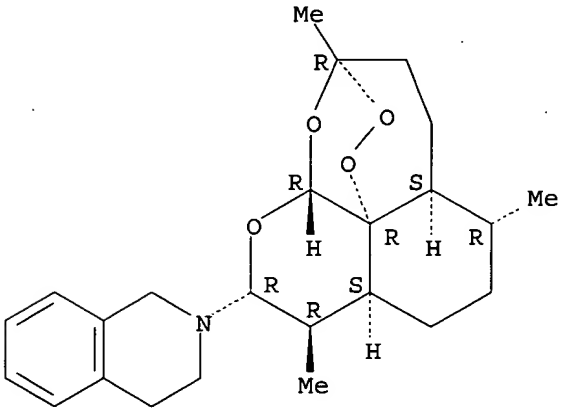
RN 255730-49-5 CAPLUS
CN 1H-Indole, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



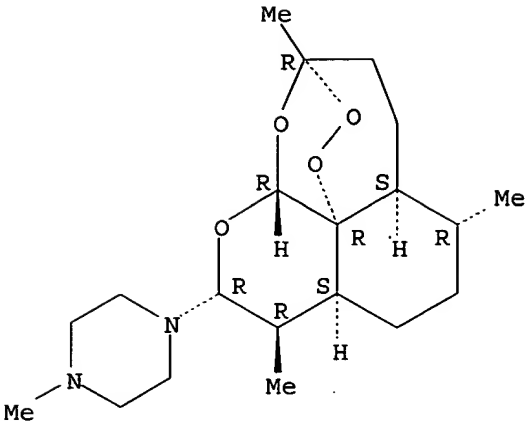
RN 255730-50-8 CAPLUS
CN Isoquinoline, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 255730-58-6 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



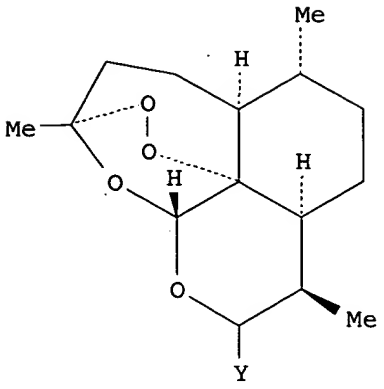
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:68459 CAPLUS
DOCUMENT NUMBER: 132:122783
TITLE: synthesis and antiparasitic activity of artemisinin derivatives (endoperoxides)
INVENTOR(S): Haynes, Richard Kingston; Chan, Ho-Wai; Lam, Wai-Lun; Tsang, Hing-Wo; Cheung, Man-Ki
PATENT ASSIGNEE(S): The Hong Kong University of Science & Technology, Peop. Rep. China
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004024	A1	20000127	WO 1999-GB2267	19990714
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2337119	AA	20000127	CA 1999-2337119	19990714
AU 9949218	A1	20000207	AU 1999-49218	19990714
BR 9912810	A	20010502	BR 1999-12810	19990714
EP 1095042	A1	20010502	EP 1999-933043	19990714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
JP 2002520416	T2	20020709	JP 2000-560130	19990714
BG 105137	A	20010831	BG 2001-105137	20010110
NO 2001000223	A	20010312	NO 2001-223	20010112

PRIORITY APPLN. INFO.: EP 1998-305596 A 19980714
WO 1999-GB2267 W 19990714

OTHER SOURCE(S): MARPAT 132:122783
GI



I

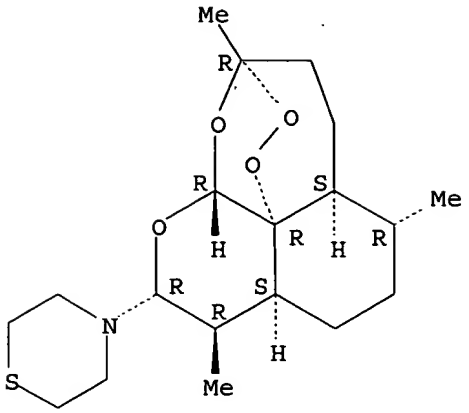
AB Synthesis of C10 substituted derivs. of artemisinin (I) [Y = halogen, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted C-linked heteroaryl, (un)substituted heterocyclylalkyl, NR1R2; R1 = H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl; R2 = (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted araalkyl; R1R2 together with the N form (un)substituted heterocycle] or a salt thereof is disclosed. Thus, I (Y = .beta.Ph) (II) is prepd. by reaction of 10-(trimethylsiloxy)dihydroartemisinin with phenylmagnesium bromide and shows good in vitro activity against chloroquinone resistant strains. I are particularly effective in the treatment of malaria, neosporosis and coccidiosis.

IT **255730-17-7P 255730-31-5P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis and antiparasitic activity of artemisinin derivs. (endoperoxides))

RN 255730-17-7 CAPLUS

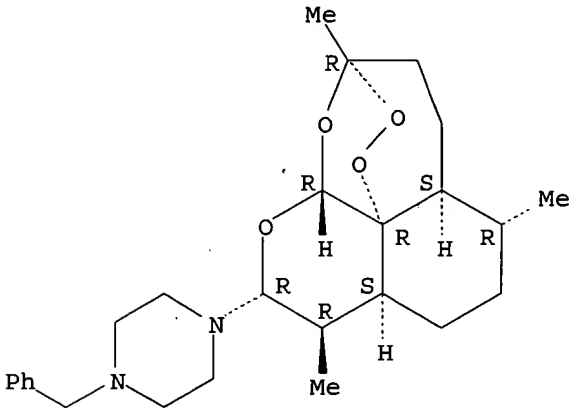
CN Thiomorpholine, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



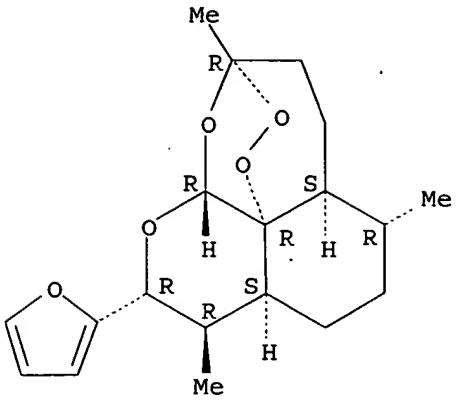
RN 255730-31-5 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



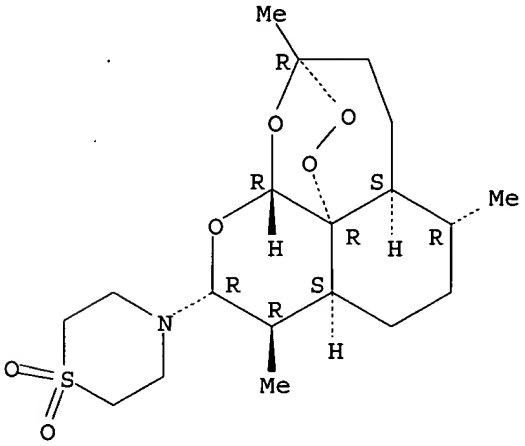
IT **204503-68-4P 255730-18-8P 255730-32-6P**
255730-33-7P 255730-47-3P 255730-49-5P
255730-50-8P 255730-58-6P 255912-96-0P
255912-97-1P 255912-98-2P 255912-99-3P
255913-00-9P 255913-02-1P 255913-03-2P
255913-04-3P 255913-05-4P 255913-06-5P
255913-07-6P 255913-08-7P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and antiparasitic activity of artemisinin derivs. (endoperoxides))
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



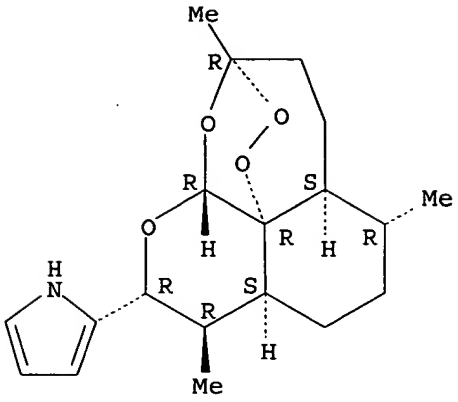
RN 255730-18-8 CAPLUS
CN Thiomorpholine, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, 1,1-dioxide (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



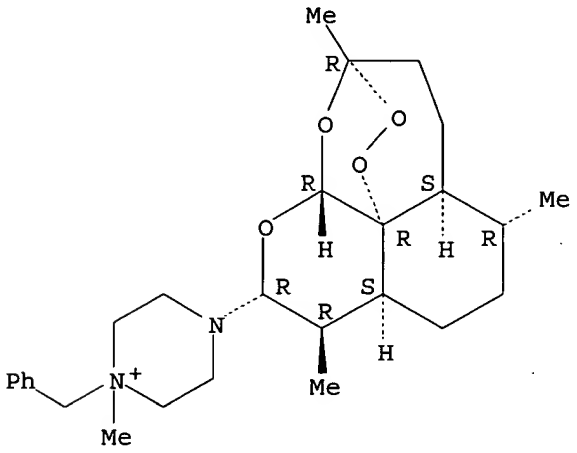
RN 255730-32-6 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 255730-33-7 CAPLUS
CN Piperazinium, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl-1-(phenylmethyl)-, iodide (9CI) (CA INDEX NAME)

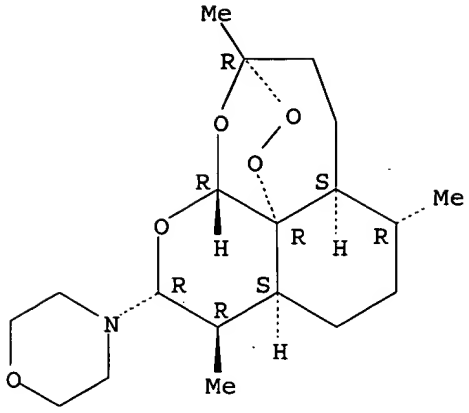
Absolute stereochemistry. Rotation (+).



● I^-

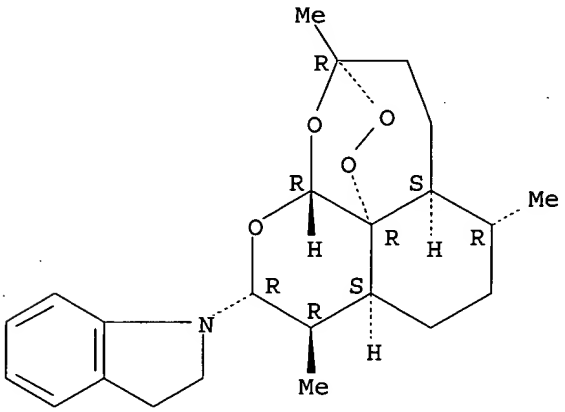
RN 255730-47-3 CAPLUS
CN Morpholine, 4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



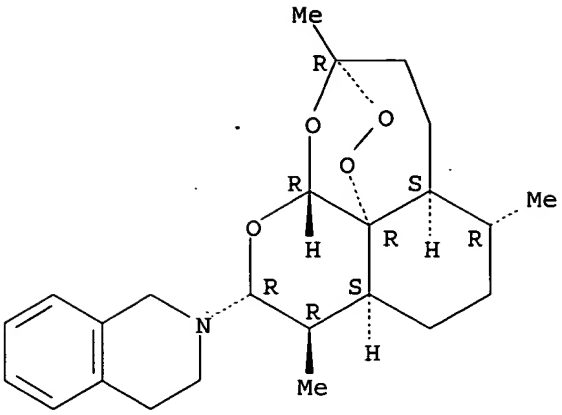
RN 255730-49-5 CAPLUS
CN 1H-Indole, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



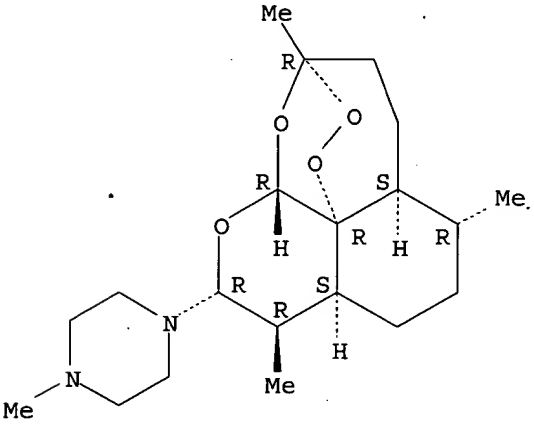
RN 255730-50-8 CAPLUS
CN Isoquinoline, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1,2,3,4-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



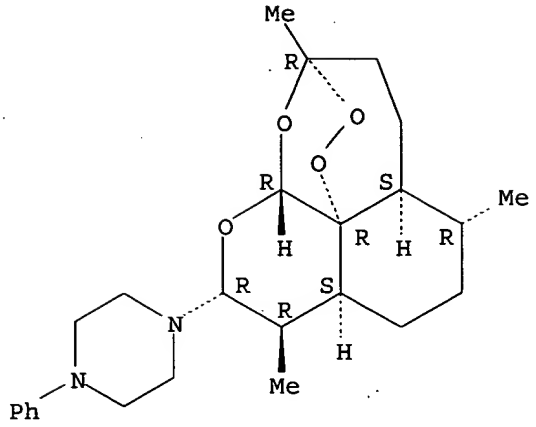
RN 255730-58-6 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



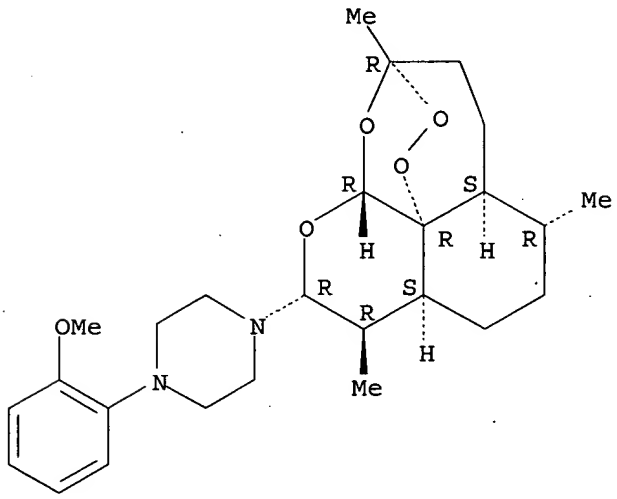
RN 255912-96-0 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



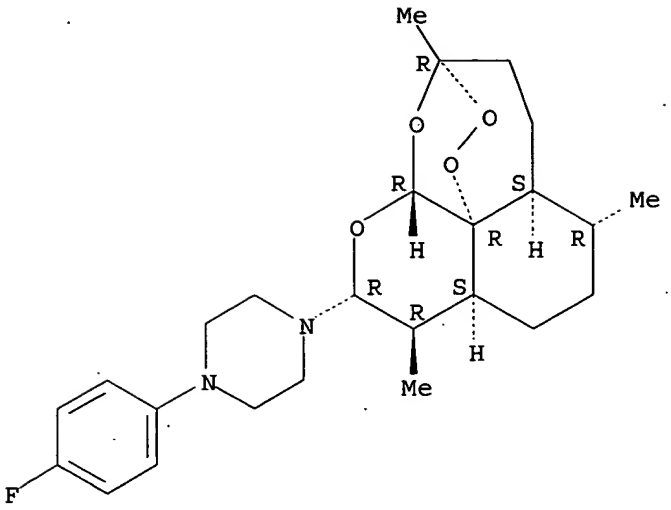
RN 255912-97-1 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(2-methoxyphenyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



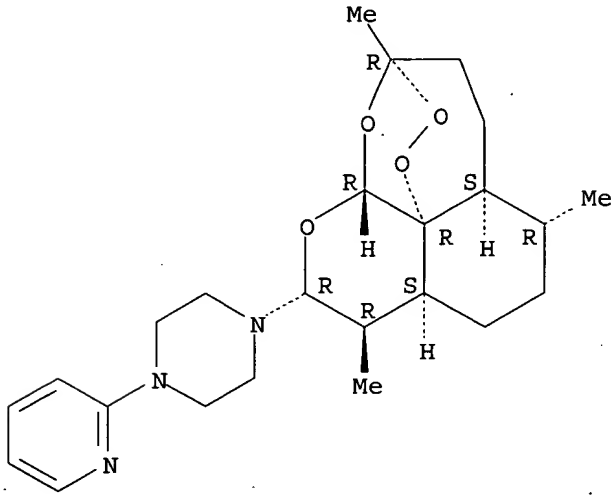
RN 255912-98-2 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(4-fluorophenyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



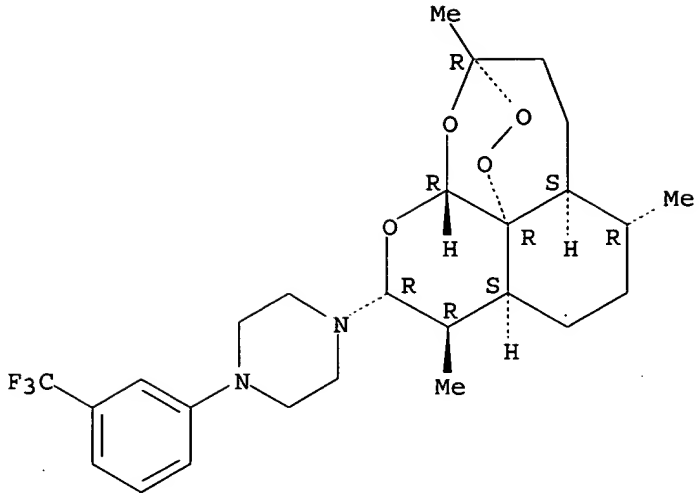
RN 255912-99-3 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



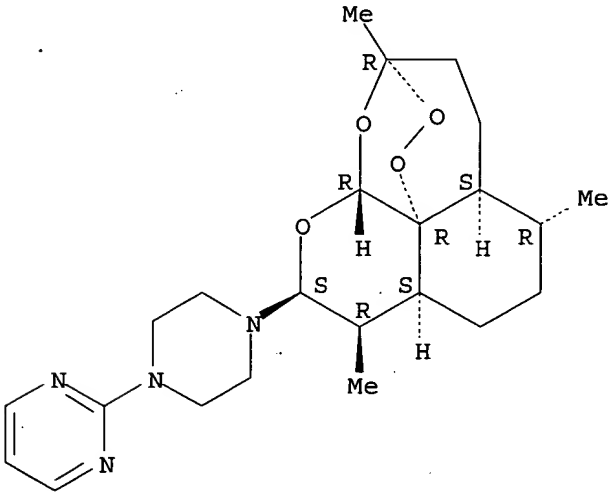
RN 255913-00-9 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



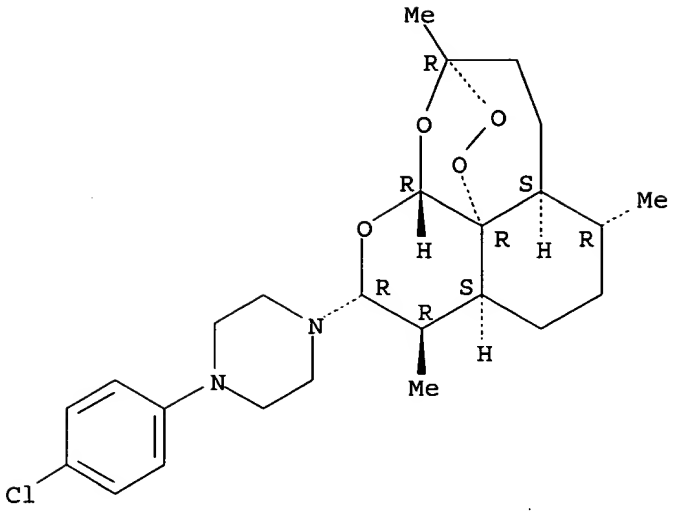
RN 255913-02-1 CAPLUS
CN Pyrimidine, 2-[4-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



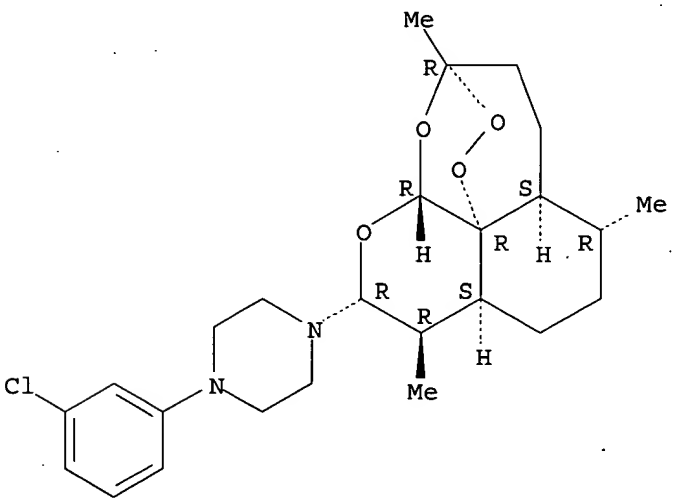
RN 255913-03-2 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



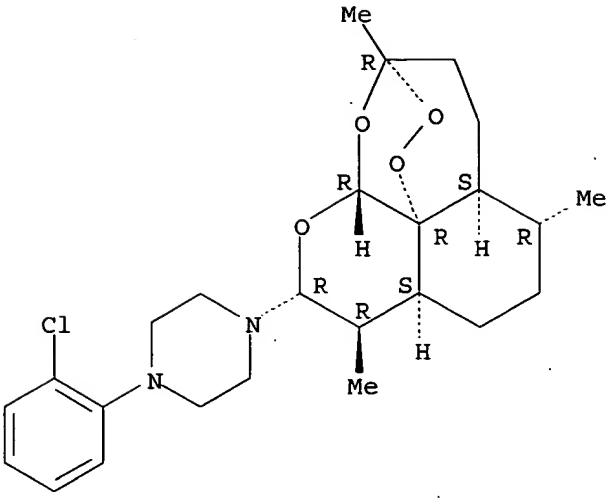
RN 255913-04-3 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



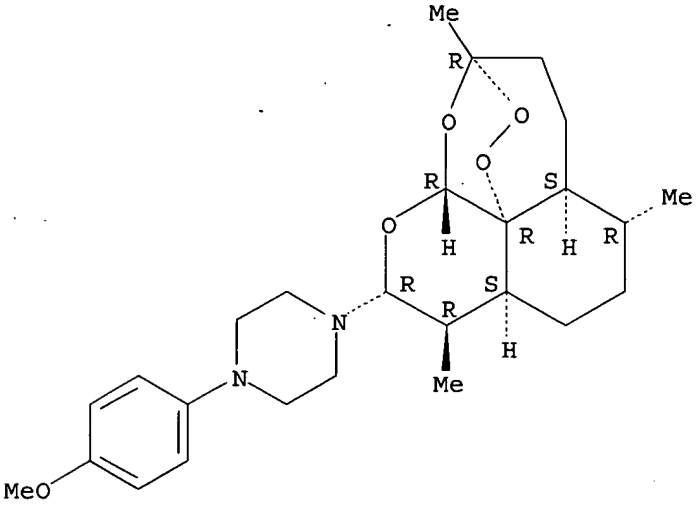
RN 255913-05-4 CAPLUS
CN Piperazine, 1-(2-chlorophenyl)-4-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



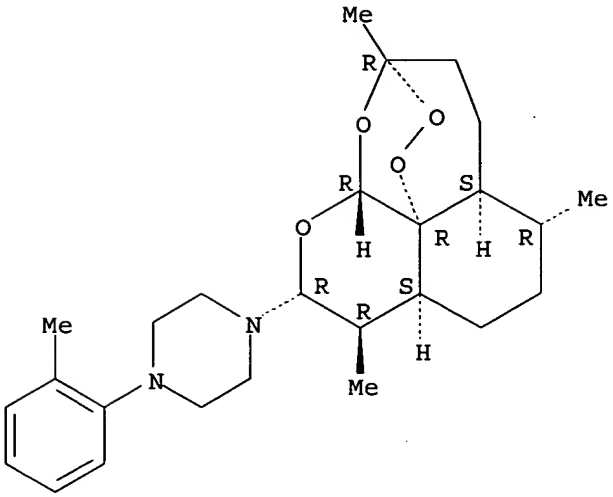
RN 255913-06-5 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(4-methoxyphenyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



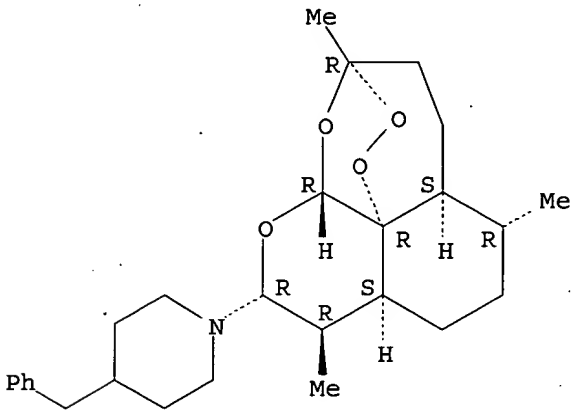
RN 255913-07-6 CAPLUS
CN Piperazine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(2-methylphenyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 255913-08-7 CAPLUS
CN Piperidine, 1-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-4-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



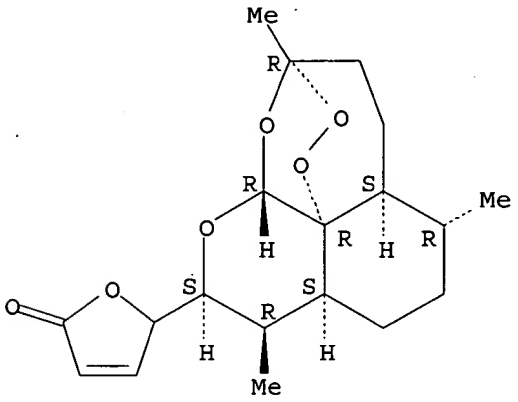
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:750915 CAPLUS
DOCUMENT NUMBER: 132:78712
TITLE: A new synthetic route to 10.beta.-alkyldeoxoartemisinins
AUTHOR(S): Ma, Jingyuan; Katz, Esther; Ziffer, Herman
CORPORATE SOURCE: Laboratory of Bioorganic Chemistry, NIDDK, Bethesda, MD, 20892, USA
SOURCE: Tetrahedron Letters (1999), 40(49), 8543-8545
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

09743827

LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:78712
AB Artemisinin was reduced with DIBAL and acetylated to yield 10.alpha.-acetoxyartemisinin. The latter compd. was treated with titanium tetrachloride and a series of trimethylsiloxyl enol ethers to produce a series of 10.beta.-alkyldeoxoartemisinins.
IT **253774-89-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 10.beta.-alkyldeoxoartemisinins)
RN 253774-89-9 CAPLUS
CN 2(5H)-Furanone, 5-[(3R,5aS,6R,8aS,9R,10S,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:629644 CAPLUS
DOCUMENT NUMBER: 132:3473
TITLE: Antimalarial, Antiproliferative, and Antitumor Activities of Artemisinin-Derived, Chemically Robust, Trioxane Dimers
AUTHOR(S): Posner, Gary H.; Ploypradith, Poonsakdi; Parker, Michael H.; O'Dowd, Hardwin; Woo, Soon-Hyung; Northrop, John; Krasavin, Mikhail; Dolan, Patrick; Kensler, Thomas W.; Xie, Suji; Shapiro, Theresa A.
CORPORATE SOURCE: Department of Chemistry School of Arts and Sciences, The Johns Hopkins University, Baltimore, MD, 21218, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(21), 4275-4280
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:3473
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

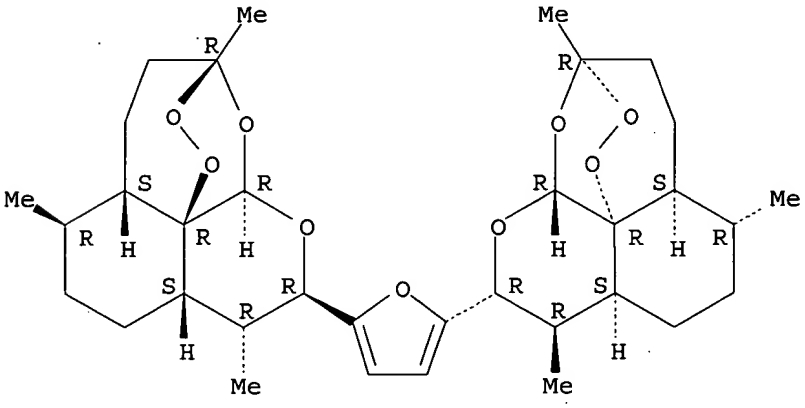
AB Nine C-10 non-acetal derivs. of the natural trioxane artemisinin (I) were prepd. as dimers using some novel chem. As designed, each dimer was stable chem. C-10 Olefinic dimers, trans,trans-, trans,cis- and cis,cis-II and C-10 satd. dimers III [X = .beta.-(1-CH2COC6H4COCH2-4)-.beta.', .beta.-(1-CH2COC6H4COCH2-3)-.beta.', .alpha.-X1-.alpha.', .alpha.-X2-.alpha.', .beta.-(1-C.tplbond.CC6H4C.tplbond.C-4)-.beta.', .beta.-(1-C.tplbond.CC6H4C.tplbond.C-3)-.beta.'] all showed good to excellent antimalarial and antiproliferative activities in vitro. Dimers III [X = .beta.-(1-CH2COC6H4COCH2-4)-.beta.', .alpha.-X1-.alpha.', .beta.-(1-C.tplbond.CC6H4C.tplbond.C-4)-.beta.'] were esp. potent and selective at inhibiting growth of some human cancer cell lines in the NCI in vitro 60-cell line assay.

IT **229981-88-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(antimalarial, antiproliferative, and antitumor activities of artemisinin non-acetal deriv. dimers)

RN 229981-88-8 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10,10'-(2,5-furandiyl)bis[decahydro-3,6,9-trimethyl-, (3R,3'R,5aS,5'aS,6R,6'R,8aS,8'aS,9R,9'R,10R,10'R,12R,12'R,12aR,12'aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

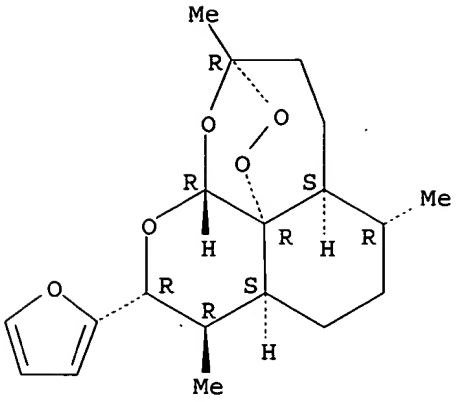


IT **204503-68-4**, 10.alpha.-(2-Furyl)-10-deoxoartemisinin
RL: RCT (Reactant); RACT (Reactant or reagent)
(antimalarial, antiproliferative, and antitumor activities of artemisinin non-acetal deriv. dimers)

RN 204503-68-4 CAPLUS

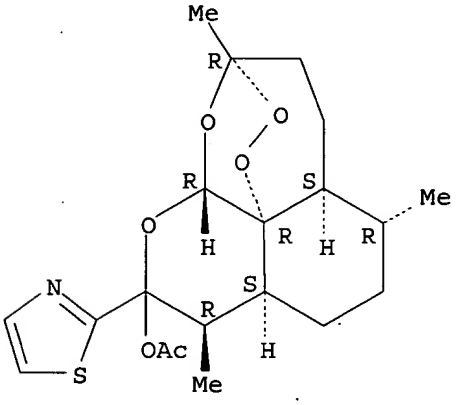
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **226952-16-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antimalarial, antiproliferative, and antitumor activities of artemisinin non-acetal deriv. dimers)
RN 226952-16-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ol, decahydro-3,6,9-trimethyl-10-(2-thiazolyl)-, acetate (ester), (3R,5aS,6R,8aS,9R,12R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:468415 CAPLUS
DOCUMENT NUMBER: 131:88067
TITLE: C-10 carbon-substituted artemisinin-like trioxane compounds having antimalarial, antiproliferative and antitumor activities
INVENTOR(S): Posner, Gary H.; Woo, Soon Hyung; Ploypradith, Poonsakdi; Parker, Michael H.; Shapiro, Theresa A.; Zheng, Qun Y.; Murray, Christopher; Daughenbaugh, Randall J.; Elias, Jeffrey S.; Northrup, John
PATENT ASSIGNEE(S): Hauser, Inc., USA; John Hopkins University
SOURCE: PCT Int. Appl., 95 pp.

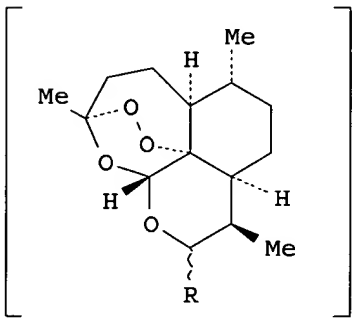
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933461	A1	19990708	WO 1998-US27717	19981230
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6156790	A	20001205	US 1997-1242	19971230
US 6160004	A	20001212	US 1998-183693	19981030
CA 2317112	AA	19990708	CA 1998-2317112	19981230
AU 9920184	A1	19990719	AU 1999-20184	19981230
AU 739687	B2	20011018		
EP 1043988	A1	20001018	EP 1998-964977	19981230
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001527043	T2	20011225	JP 2000-526218	19981230

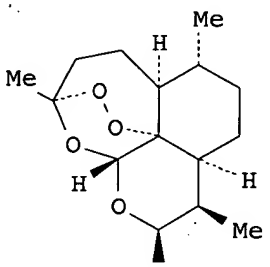
PRIORITY APPLN. INFO.: US 1997-1242 A 19971230
US 1998-183693 A 19981030
WO 1998-US27717 W 19981230

OTHER SOURCE(S): MARPAT 131:88067

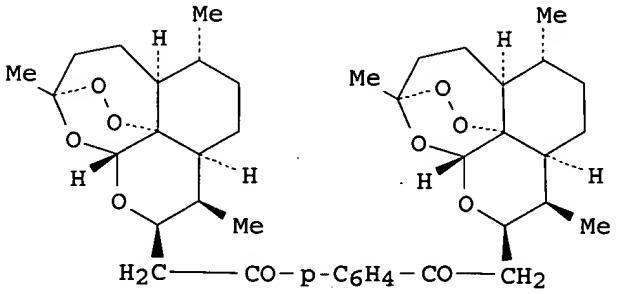
GI



x I



II



III

AB The title compds. [I; x = 1, 2, 3; R = (un)substituted aryl, heteroaryl, acetylenic, polyethylene glycol, aroylmethylene, alkanoylmethylene, alkenyl, diketone, polyethylene glycol, bisacetylene, alkyl, bisacetylene,

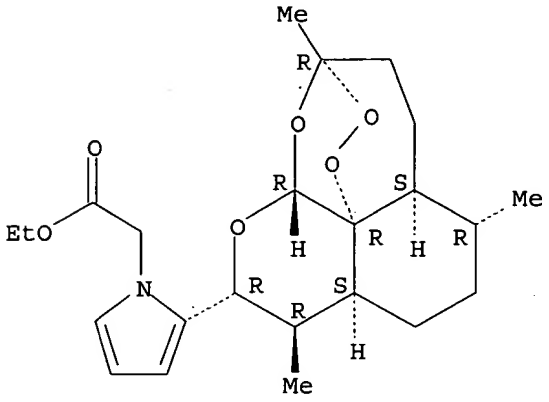
etc.] are prepd. Thus, .beta.-artemether (II) reacted with 1,4-bis[1-(trimethylsilyloxy)vinyl]benzene (also prepd.) in CH2Cl2 contg. 1M soln. of TiCl4 at -78.degree. for 1 h to give 13% III, whose antimalarial activity was ca. 5 times that of artemisinin.

IT **220115-05-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of antimalarial and antiproliferative C-10 carbon-substituted artemisinin-like trioxane compds.)

RN 220115-05-9 CAPLUS

CN 1H-Pyrrole-1-acetic acid, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **193348-60-6P 204503-67-3P 204503-68-4P**
220114-93-2P 220114-96-5P 220114-98-7P
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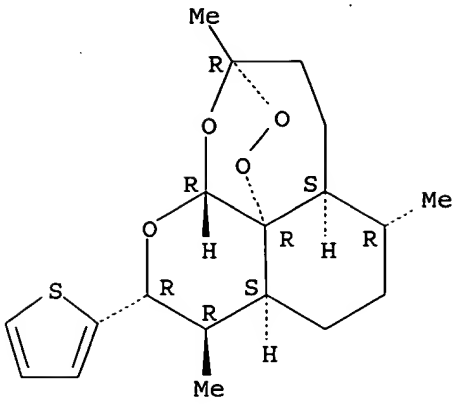
220115-08-2P 229981-72-0P 229981-75-3P
229981-76-4P 229981-88-8P 229981-89-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antimalarial and antiproliferative C-10 carbon-substituted artemisinin-like trioxane compds.)

RN 193348-60-6 CAPLUS

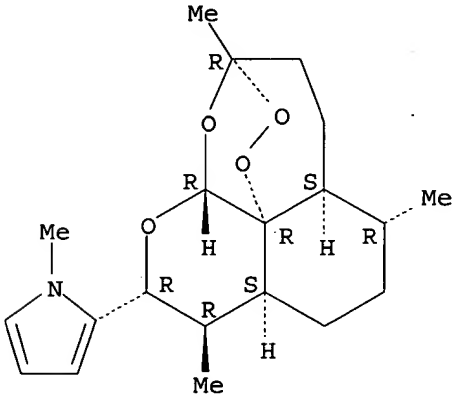
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(2-thienyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



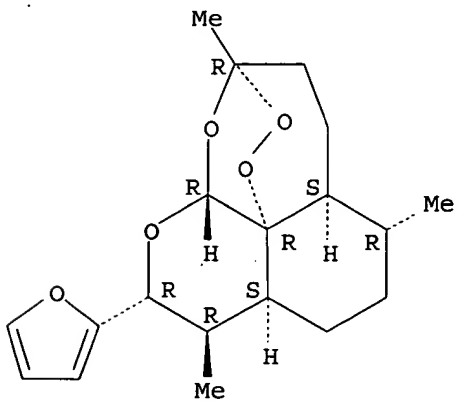
RN 204503-67-3 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

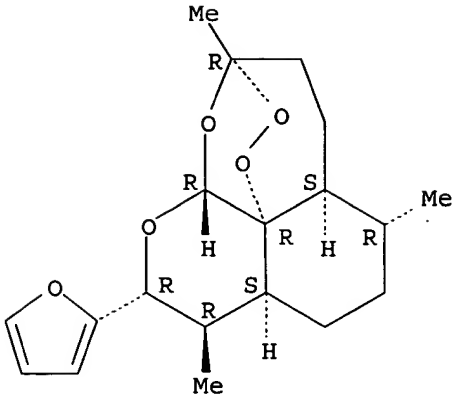
Absolute stereochemistry. Rotation (+).



RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

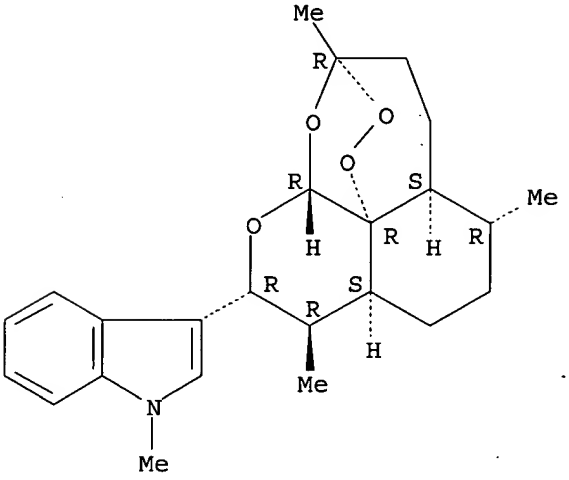
Absolute stereochemistry. Rotation (+).





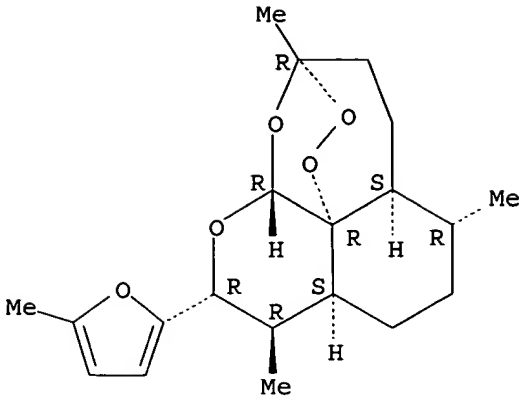
RN 220114-93-2 CAPLUS
CN 1H-Indole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



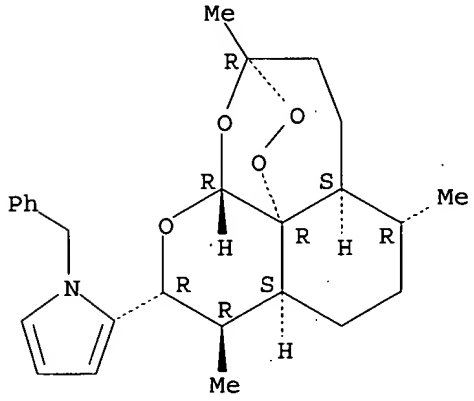
RN 220114-96-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(5-methyl-2-furanyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



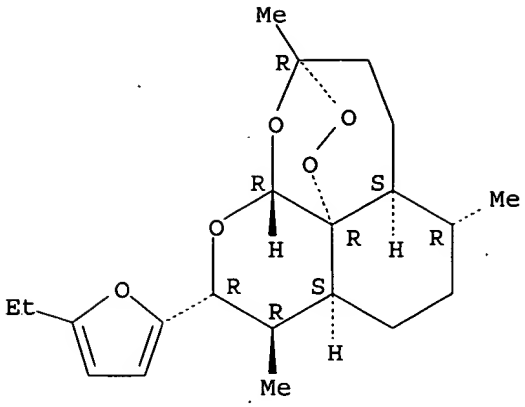
RN 220114-98-7 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



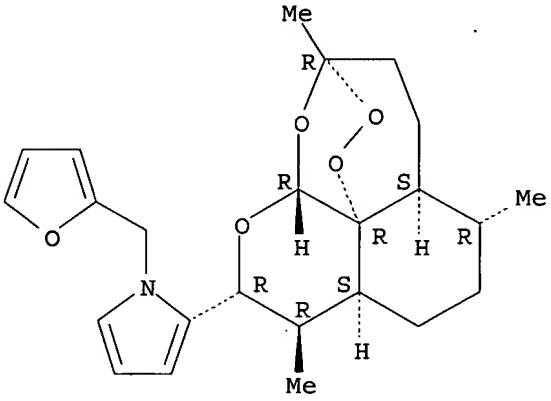
RN 220115-00-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(5-ethyl-2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



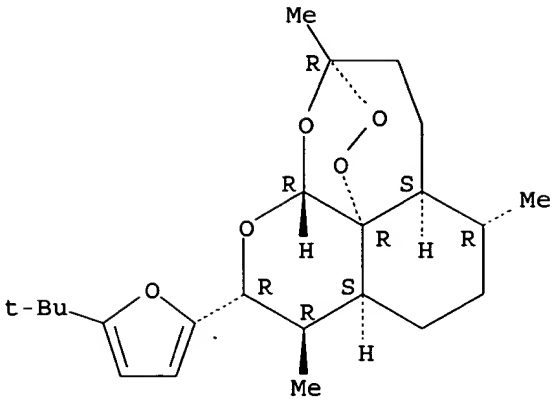
RN 220115-01-5 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(2-furanylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



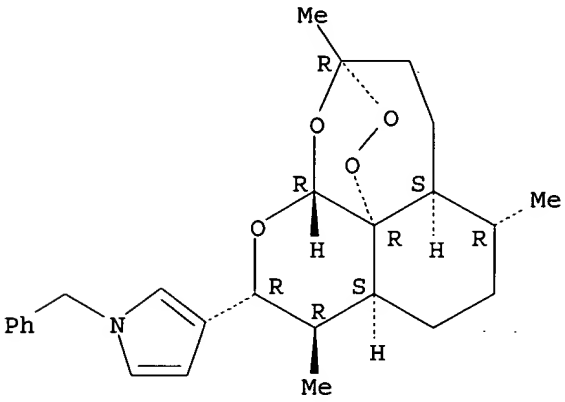
RN 220115-04-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-[5-(1,1-dimethylethyl)-2-furanyl]decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



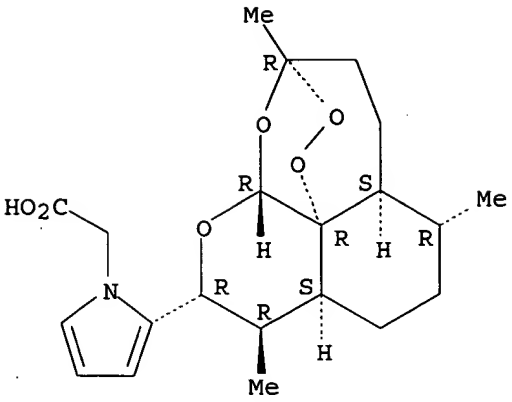
RN 220115-08-2 CAPLUS
CN 1H-Pyrrole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



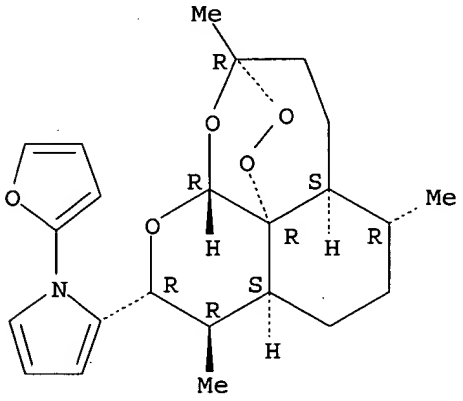
RN 229981-72-0 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



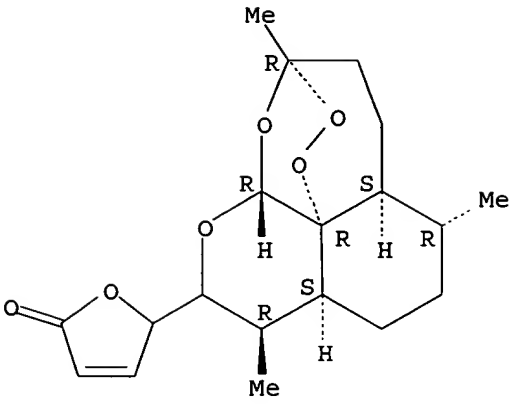
RN 229981-75-3 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(2-furanyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



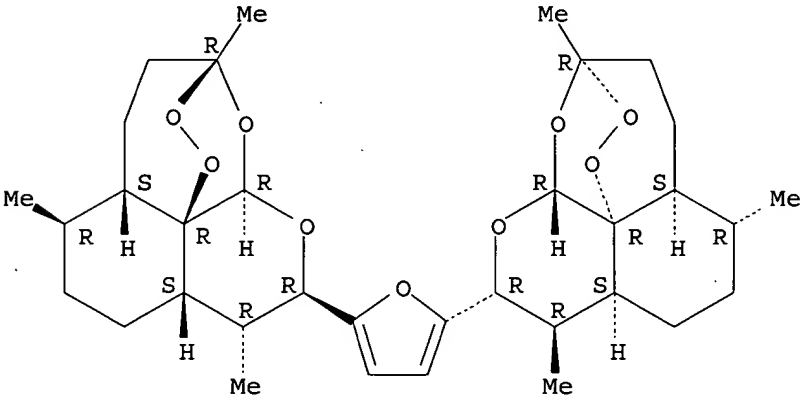
RN 229981-76-4 CAPLUS
CN 2(5H)-Furanone, 5-[(3R,5aS,6R,8aS,9R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



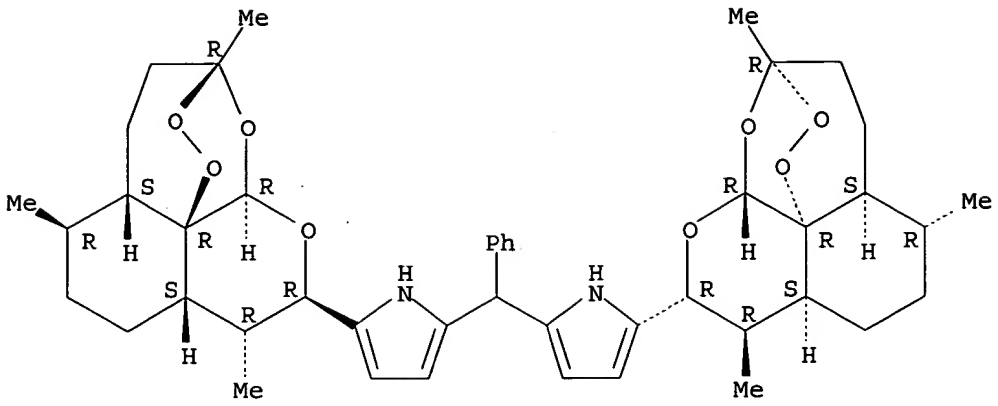
RN 229981-88-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10,10'-(2,5-furandiyl)bis[decahydro-3,6,9-trimethyl-, (3R,3'R,5aS,5'aS,6R,6'R,8aS,8'aS,9R,9'R,10R,10'R,12R,12'R,12aR,12'aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 229981-89-9 CAPLUS
CN 1H-Pyrrole, 2,2'-(phenylmethylene)bis[[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

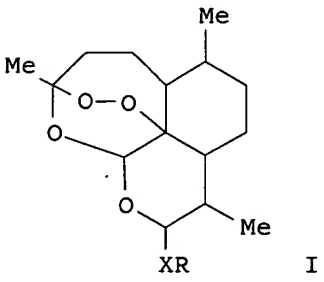


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:234337 CAPLUS
DOCUMENT NUMBER: 130:267461
TITLE: Preparation of artemisin derivative containing phenyl and heterocyclic radicals
INVENTOR(S): Li, Yang; Yang, Yonghua; Liang, Jie; Shan, Feng; Wu, Guangshao
PATENT ASSIGNEE(S): Shanghai Inst. of Materia Medica, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 17 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1122806	A	19960522	CN 1994-113982	19941109
CN 1049435	B	20000216		

PRIORITY APPLN. INFO.: CN 1994-113982 19941109
OTHER SOURCE(S): CASREACT 130:267461; MARPAT 130:267461
GI



I

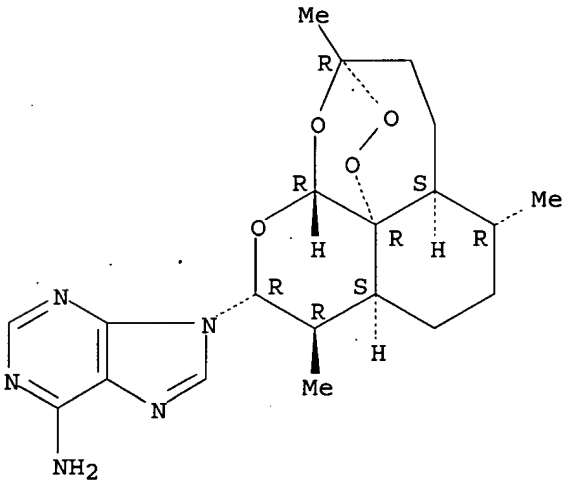
AB Title artemisin derivs. [I; X = O, NH; R = Ph, R3 substituted Ph, 2 same or different R3 and R4 substituted Ph, the heterocyclic radical is alkali

adenyl, thymine, cytimidine, uracil, and their R3 substituted groups, triazo-, and CONH2 or R3 substituted triazo-; R3 = R4 = hydroxy, alkoxy (C1-C4), alkyl (C1-C4), COOCH3, COOC2H5, NHCOCH3, nitro, halogen (F, Cl, Br, I), dihydrogen artemisin radical] are prepd. by reaction of dihydrogen artemisin, dihydrogen artemisin acetate, dihydrogen artemisin trifluoroacetate, and anilines with R3 substituted groups, R3 or R3 and R4 substituted phenols, Ph compd., heterocyclic compd. or its silicone ether derivs. in the presence of acidic catalyst, boron trifluoride etherate, SnCl4, TiCl4, trifluoroacetic acid, p-Me benzenesulfonic acid, trimethylsilyl triflate, H2SO4 and H3PO4 and polar solvent, alkyl halide, Et ether, acetonitrile, THF, pyridine, triethylamine, and methyl-sulfoxide at -10.degree. to 40.degree.. Phenylamino artemisin, 3-chloro-phenylamino artemisin, 4-artemisin, 3-nitro-phenoxy artemisin, 4- methoxy-phenoxy artemisin, 4-(methoxycarbonyl)-phenoxy artemisin, 4-acetamino-phenoxy artemisin, tris(artemisin) phloroglucin, 5- hydroxy-1,3-bis(artemisin) benzenediol, adenyl artemisin, 5- fluoro-uracil artemisin, 3-aminocarbonyl triazo artemisin, and 2,4- dimethoxyphenyl artemisin were prepd. as antitumor, antiviral, and antiparasitic agents.

IT **221890-88-6P 221890-89-7P 221890-90-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of artemisin derivs. as antibiotics and antitumor agents)

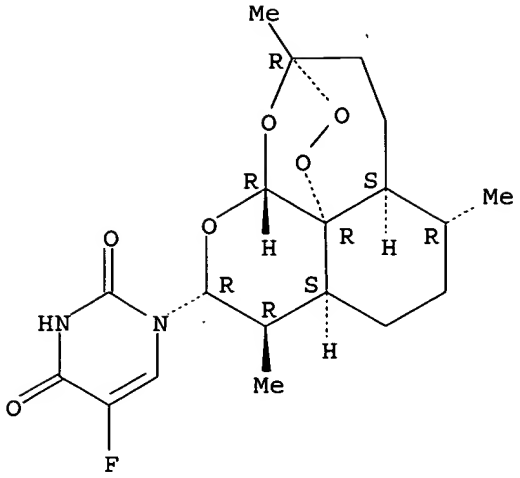
RN 221890-88-6 CAPLUS
CN 9H-Purin-6-amine, 9-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



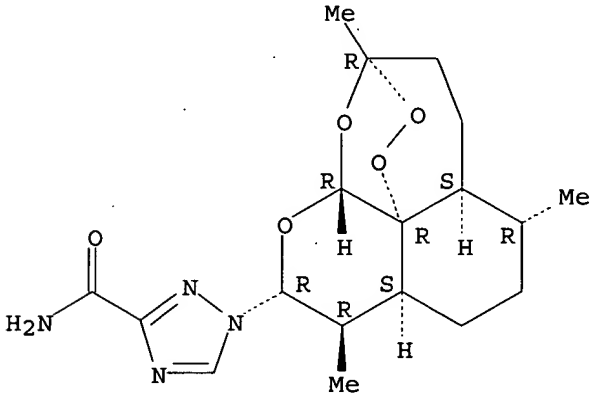
RN 221890-89-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-fluoro-9-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



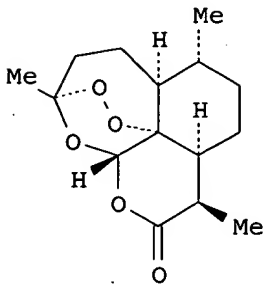
RN 221890-90-0 CAPLUS
CN 1H-1,2,4-Triazole-3-carboxamide, 9-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

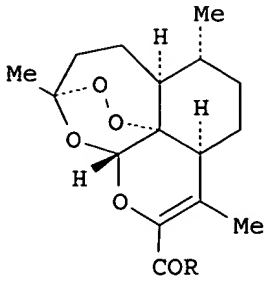


L4 ANSWER 21 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:210851 CAPLUS
DOCUMENT NUMBER: 131:32059
TITLE: Antimalarial artemisinin analogs. Synthesis via chemoselective C-C bond formation and preliminary biological evaluation
AUTHOR(S): O'Dowd, Hardwin; Ploypradith, Poonsakdi; Xie, Suji; Shapiro, Theresa A.; Posner, Gary H.
CORPORATE SOURCE: Department of Chemistry, School of Arts and Sciences, The Johns Hopkins University, Baltimore, MD, 21218, USA
SOURCE: Tetrahedron (1999), 55(12), 3625-3636
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:32059
GI



I



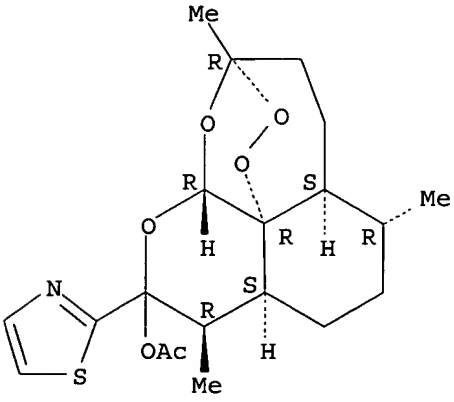
II

AB The peroxide bond in artemisinin trioxane lactone I withstood exposure to lithiothiazole and to lithiobenzothiazole; nucleophilic addn. of these powerful organometallic reagents to only the lactone carbonyl group was obsd. Trioxane aldehyde II (R = H) reacted with organolithium, Grignard, and phosphorus ylide nucleophiles exclusively via carbonyl addn. Trioxane ketone II (R = Ph) reacted with phenyllithium via only carbonyl addn. These chemoselective lactone, aldehyde, and ketone carbonyl addn. reactions produced a series of new, enantiomerically pure, C-10 non-acetal derivs. of natural trioxane artemisinin having high in vitro antimalarial potencies.

IT **226952-16-5P 226952-32-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and antimalarial activity of artemisinin analogs)

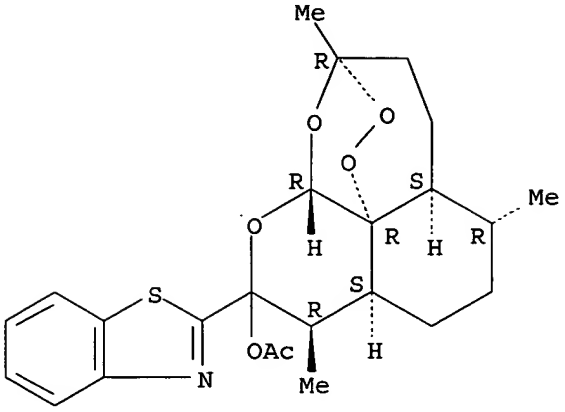
RN 226952-16-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ol, decahydro-3,6,9-trimethyl-10-(2-thiazolyl)-, acetate (ester), (3R,5aS,6R,8aS,9R,12R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



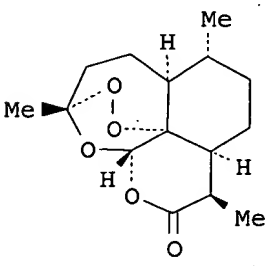
RN 226952-32-5 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-ol, 10-(2-benzothiazolyl)decahydro-3,6,9-trimethyl-, acetate (ester), (3R,5aS,6R,8aS,9R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

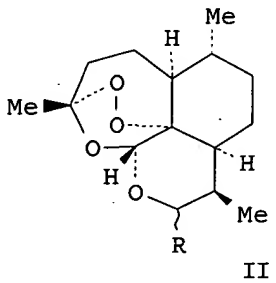


REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:3589 CAPLUS
DOCUMENT NUMBER: 130:139466
TITLE: Orally Active, Hydrolytically Stable, Semisynthetic, Antimalarial Trioxanes in the Artemisinin Family
AUTHOR(S): Posner, Gary H.; Parker, Michael H.; Northrop, John; Elias, Jeffrey S.; Ploypradith, Poonsakdi; Xie, Suji; Shapiro, Theresa A.
CORPORATE SOURCE: Department of Chemistry School of Arts and Sciences, The Johns Hopkins University, Baltimore, MD, 21218, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(2), 300-304
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB In only three chem. operations, natural trioxane lactone artemisinin (I) was converted into a series of C-10 carbon-substituted 10-deoxoartemisinin compds. II [R = {C6H3(OMe)2-2,4}-.alpha., {C6H3(OCH2CH:CH2)2-2,4}-.alpha., {C6H2(OMe)3-2,4,6}-.alpha., .alpha.-(2,3-dimethoxy-2-naphthyl), .alpha.-(2-furyl), .alpha.-(5-methyl-2-furyl), .alpha.-(5-ethyl-2-furyl),

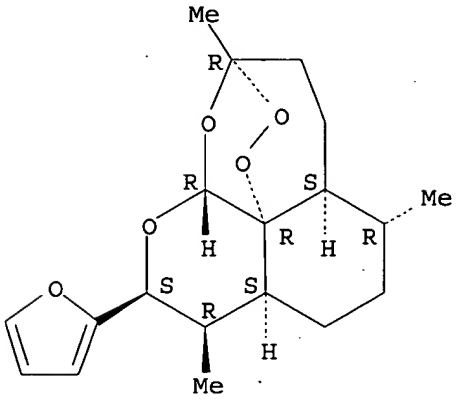
.alpha.-(5-tert-butyl-2-furyl), .alpha.-(2-thienyl), .alpha.-(1-methylindol-3-yl), .alpha.-(1-benzylpyrrol-2-yl), .alpha.-{1-(2-furylmethyl)pyrrol-2-yl}, .alpha.-{1-(ethoxycarbonylmethyl)pyrrol-2-yl}, .beta.-(4-chlorophenylethynyl), .beta.-(4-fluorophenylethynyl), .beta.-{4-(methylthio)phenylethynyl}]. The three steps involved lactone redn., replacement of the anomeric lactol OH by F using diethylaminosulfur trifluoride, and finally boron trifluoride-promoted substitution of F by aryl, heteroaryl, and acetylide nucleophiles. All of these C-10 nonacetal, chem. robust, enantiomerically pure compds. II have high antimalarial potencies in vitro against Plasmodium falciparum malaria parasites, and furans II (R = 2-furyl, 5-methyl-2-furyl) and pyrrole II (R = N-methylpyrrol-2-yl) are antimalarially potent also in vivo even when administered to rodents orally.

IT **220115-07-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BYP (Byproduct); BIOL (Biological study); PREP (Preparation)
(prepn. and antimalarial activity of aryl, heteroaryl and arylethynyl trioxane analogs of artemisinin)

RN 220115-07-1 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10S,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

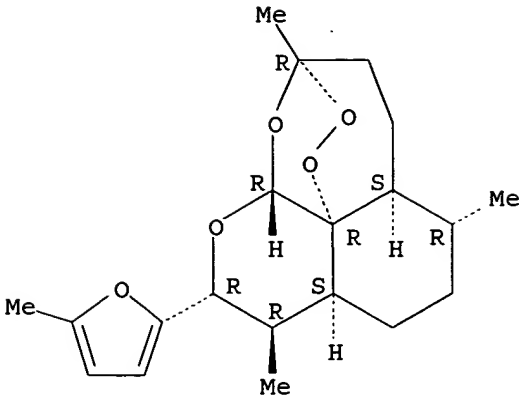


IT **220114-96-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and antimalarial activity of aryl, heteroaryl and arylethynyl trioxane analogs of artemisinin)

RN 220114-96-5 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(5-methyl-2-furanyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

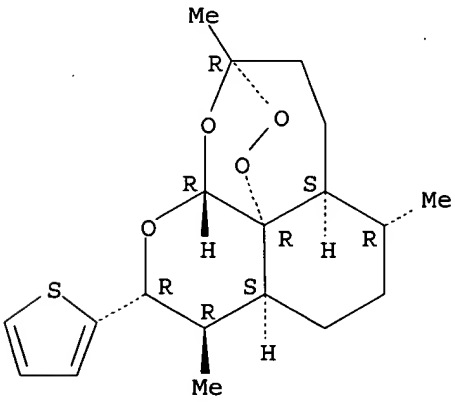
Absolute stereochemistry. Rotation (+).



IT **193348-60-6P**, 10.alpha.-(2-Thienyl)-10-deoxoartemisinin
204503-67-3P, 10.alpha.-(1-Methylpyrrol-2-yl)-10-deoxoartemisinin
204503-68-4P, 10.alpha.-(2-Furyl)-10-deoxoartemisinin
220114-93-2P, 10.alpha.-(1-Methylindol-3-yl)-10-deoxoartemisinin
220114-98-7P, 10.alpha.-(1-Benzylpyrrol-2-yl)-10-deoxoartemisinin
220115-00-4P 220115-01-5P 220115-04-8P
220115-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antimalarial activity of aryl, heteroaryl and arylethynyl trioxane analogs of artemisinin)

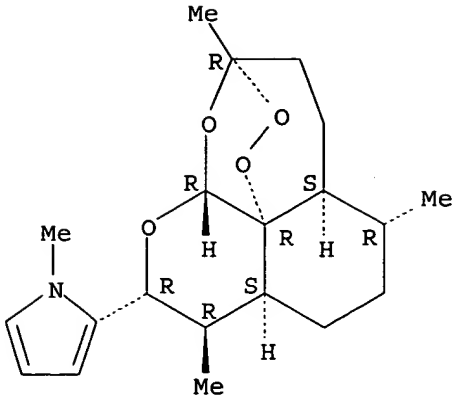
RN 193348-60-6 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(2-thienyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



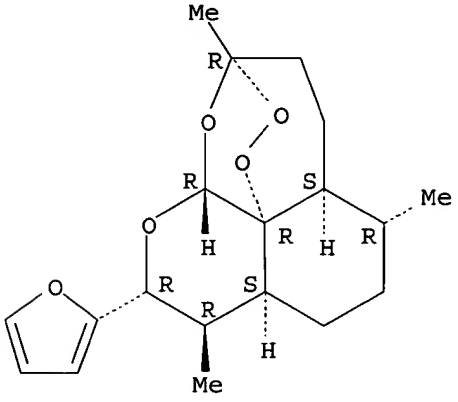
RN 204503-67-3 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



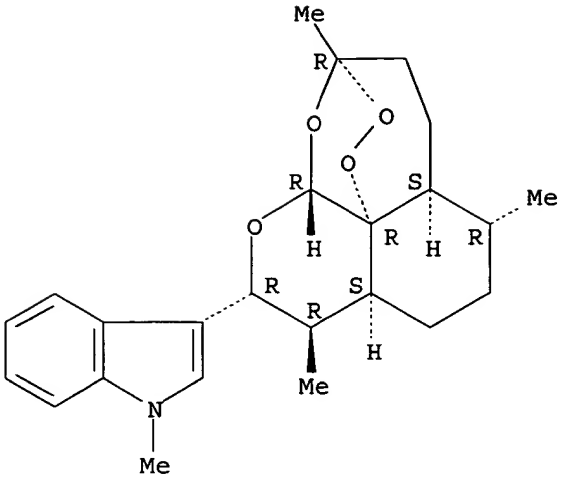
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



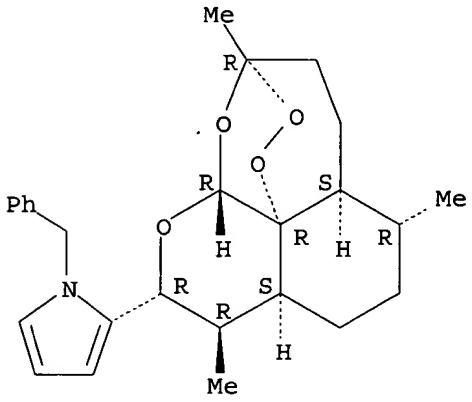
RN 220114-93-2 CAPLUS
CN 1H-Indole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



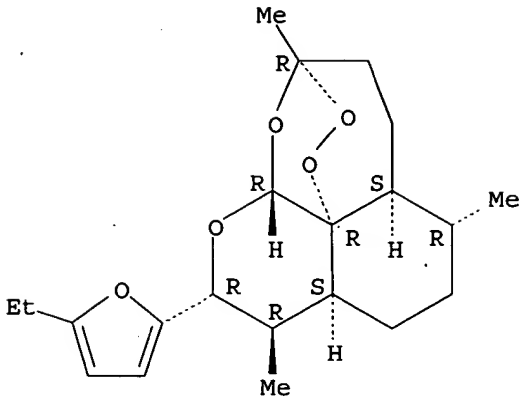
RN 220114-98-7 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



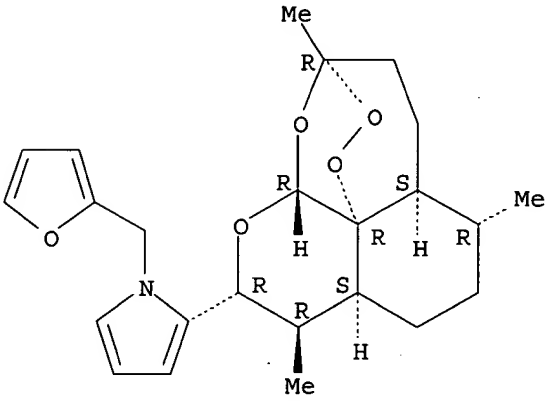
RN 220115-00-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(5-ethyl-2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



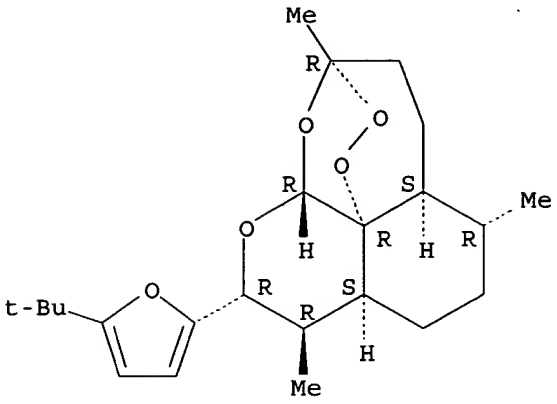
RN 220115-01-5 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(2-furanylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



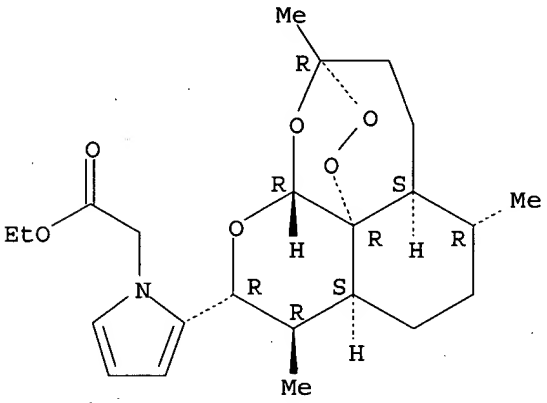
RN 220115-04-8 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-[5-(1,1-dimethylethyl)-2-furanyl]decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



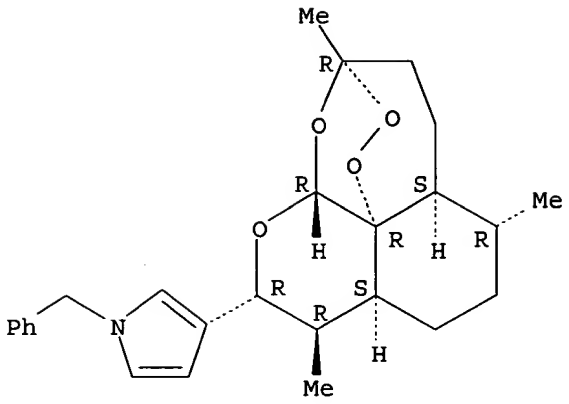
RN 220115-05-9 CAPLUS
CN 1H-Pyrrole-1-acetic acid, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **220115-08-2P**
RL: BYP (Byproduct); PREP (Preparation)
(prepn. and antimalarial activity of aryl, heteroaryl and arylethynyl trioxane analogs of artemisinin)
RN 220115-08-2 CAPLUS
CN 1H-Pyrrole, 3-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-(phenylmethyl)-(9CI) (CA INDEX NAME)

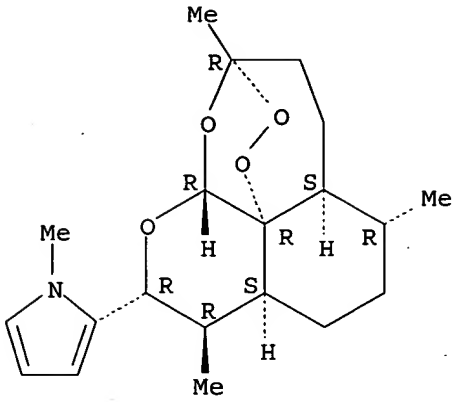
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

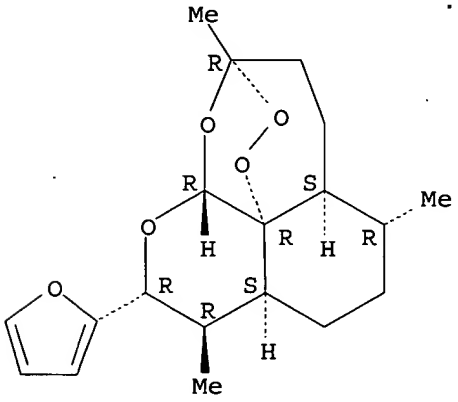
L4 ANSWER 23 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:159576 CAPLUS
DOCUMENT NUMBER: 128:230529
TITLE: Direct conversion of pyranose anomeric OH.fwdarw.F.fwdarw.R in the artemisinin family of antimalarial trioxanes
AUTHOR(S): Woo, Soon Hyung; Parker, Michael H.; Ploypradith, Poonsakdi; Northrop, John; Posner, Gary H.
CORPORATE SOURCE: Research Institute of Industrial Science and Technology, Pohang, 790-600, S. Korea
SOURCE: Tetrahedron Letters (1998), 39(12), 1533-1536
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:230529
AB Eleven examples form the basis of a short and effective synthetic method for replacement of an anomeric fluorine atom by satd., unsatd., aryl and heteroaryl carbon nucleophiles to prep. .alpha.- or .beta.-oriented C10-R derivs. of the trioxane 10-deoxoartemisinin.
IT **204503-67-3P 204503-68-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of substituted deoxoartemisinins)
RN 204503-67-3 CAPLUS
CN 1H-Pyrrole, 2-[(3R,5aS,6R,8aS,9R,10R,12R,12aR)-decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



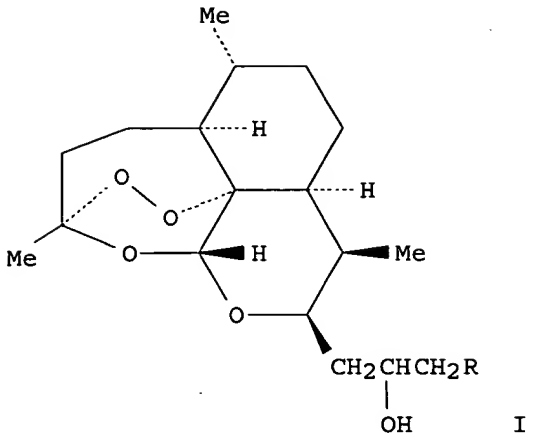
RN 204503-68-4 CAPLUS
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-(2-furanyl)decahydro-3,6,9-trimethyl-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:526864 CAPLUS
DOCUMENT NUMBER: 127:190855
TITLE: Synthesis of new artemisinin derivatives containing C-C bond at position 12. 1. New route to 12-deoxoartemisinin derivatives containing nitrogen
AUTHOR(S): Mai, Van Tri; Nguyen, Van Tuyen; Pham, Van Cuong
CORPORATE SOURCE: Dept. Chem., National Center for Natural Science and Technol. of Vietnam, Vietnam
SOURCE: Tap Chi Hoa Hoc (1997), 35(1), 11-13
CODEN: TCHHDC; ISSN: 0378-2336
PUBLISHER: Toa Soan Tap Chi Hoa Hoc
DOCUMENT TYPE: Journal
LANGUAGE: Vietnamese
GI



I

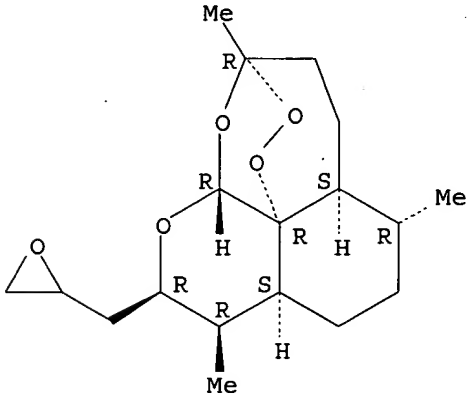
AB Synthesis of new derivs. of artemisinin contg. a carbon-carbon bond at position 12 I (R = morpholino, 4-(4-fluorophenyl)piperazino) is described.

IT **194409-61-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 12-deoxoartemisinin derivs. contg. nitrogen)

RN 194409-61-5 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(oxiranylmethyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

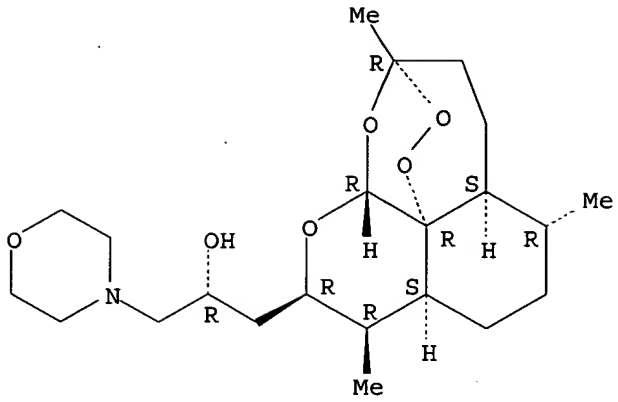


IT **194409-62-6P 194409-63-7P 194409-64-8P**
194409-65-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 12-deoxoartemisinin derivs. contg. nitrogen)

RN 194409-62-6 CAPLUS

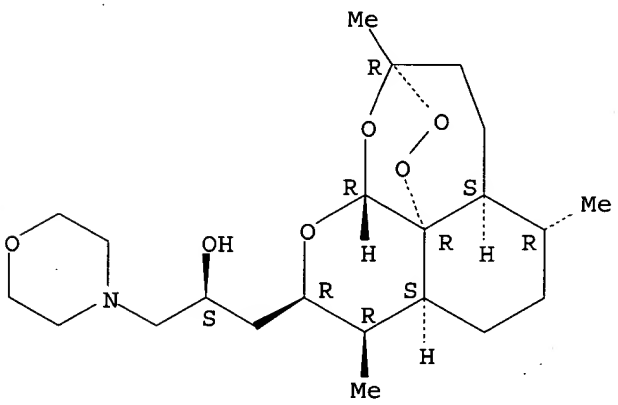
CN 4-Morpholineethanol, .alpha.-[(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl)methyl]-, [3R-[3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.(R*),12.beta.,12aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



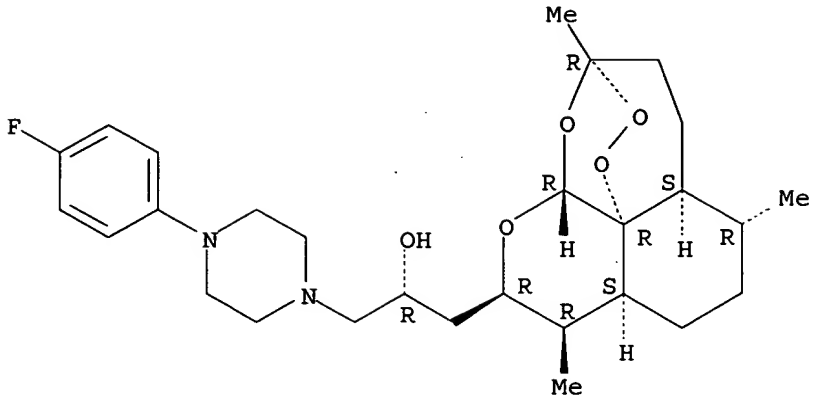
RN 194409-63-7 CAPLUS
CN 4-Morpholineethanol, .alpha.-[(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl)methyl]-, [3R-[3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.(S*),12.beta.,12aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



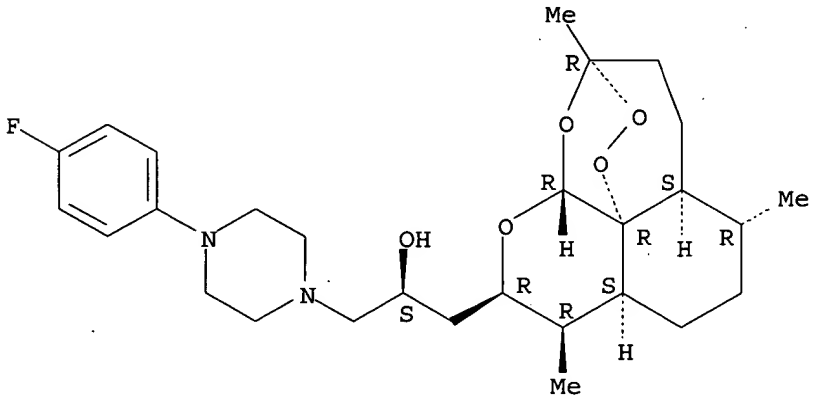
RN 194409-64-8 CAPLUS
CN 1-Piperazineethanol, .alpha.-[(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl)methyl]-4-(4-fluorophenyl)-, [3R-[3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.(R*),12.beta.,12aR*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

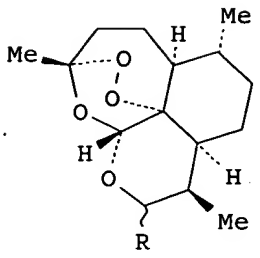


RN 194409-65-9 CAPLUS
CN 1-Piperazineethanol, .alpha.-[(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl)methyl]-4-(4-fluorophenyl)-, [3R-[3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.(S*),12.beta.,12aR*]]- (9CI) (CA INDEX NAME)

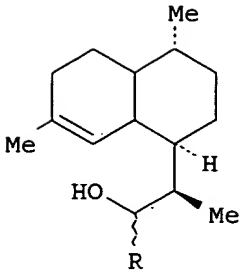
Absolute stereochemistry.



L4 ANSWER 25 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:439312 CAPLUS
DOCUMENT NUMBER: 127:149262
TITLE: A concise synthesis of novel aromatic analogs of artemisinin
AUTHOR(S): Jung, Mankil; Lee, Seokjoon
CORPORATE SOURCE: Department of Chemistry, Yonsei University, Seoul, S. Korea
SOURCE: Heterocycles (1997), 45(6), 1055-1058
CODEN: HTCYAM; ISSN: 0385-5414
PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:149262
GI



I



II

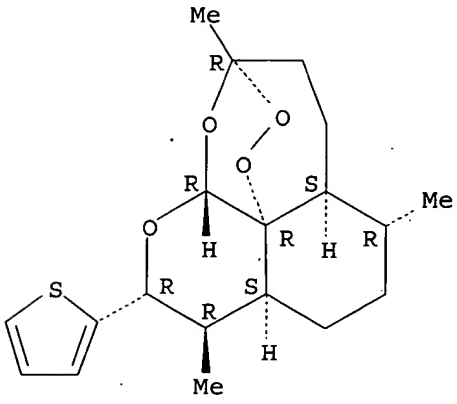
AB Arom. analogs I [R = .beta.-CH2(C6H4CH:CH2-3), .beta.-CH2(C6H4CO2H-3), .beta.-CH2(C6H4Cl-2), CH2(C6H4OMe-4), .alpha.-(2-thienyl)] of deoxoartemisinin were prepd. from artemisinic acid via photooxygenative cyclization of II [R = CH2(C6H4CH:CH2-3), CH2(C6H4CO2H-3), CH2(C6H4Cl-2), CH2(C6H4OMe-4), (2-thienyl)] as a key step. Arom. analogs with electron-donating substituents show 5-8 more in vitro antimalarial activity compared to artemisinin.

IT **193348-60-6P**, 12.alpha.-(2-Thienyl)deoxoartemisinin
193348-67-3P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(concise synthesis of novel arom. analogs of artemisinin as antimalarials)

RN 193348-60-6 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(2-thienyl)-, (3R,5aS,6R,8aS,9R,10R,12R,12aR)- (9CI) (CA INDEX NAME)

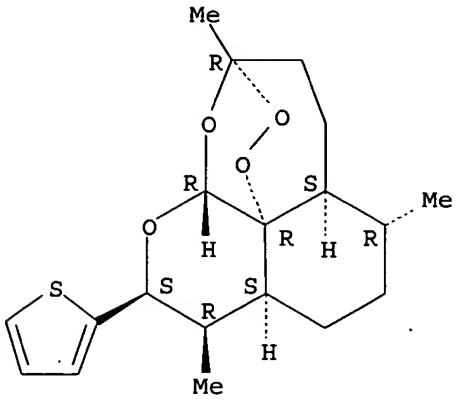
Absolute stereochemistry. Rotation (+).



RN 193348-67-3 CAPLUS

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-3,6,9-trimethyl-10-(2-thienyl)-, [3R-(3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.,12.beta.,12aR*)]- (9CI) (CA INDEX NAME)

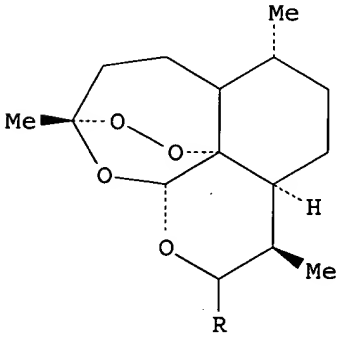
Absolute stereochemistry.



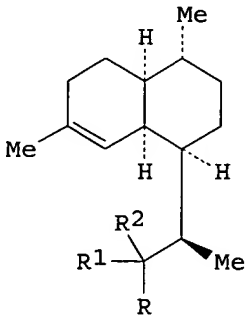
L4 ANSWER 26 OF 26 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:650206 CAPLUS
DOCUMENT NUMBER: 119:250206
TITLE: Preparation of (+)-deoxoartemisinin analogs as antimalarials
INVENTOR(S): McChesney, James D.; Jung, Mankil
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5225562	A	19930706	US 1990-565470	19900810

PRIORITY APPLN. INFO.: US 1990-565470 19900810
OTHER SOURCE(S): MARPAT 119:250206
GI



I



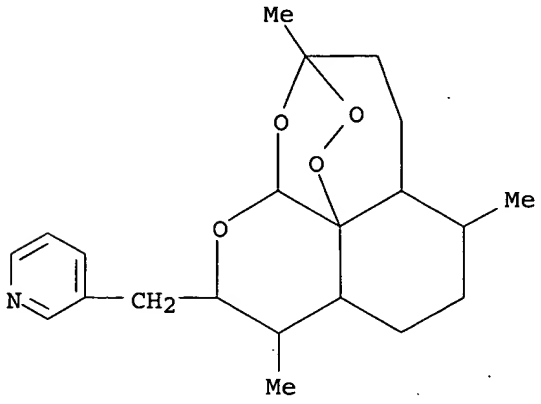
II

AB Title compds. [I; R = H, (cyclo)alkyl, hydroxyalkyl, aryl, etc.] were prepd. as antimalarials (no data). Thus, artemisinic acid (isolation from Artemisia annua leaves given) was esterified and the product reduced to give aldehyde II (R = H; R1R2 = O) which was condensed with the Grignard reagent prepd. from BuBr to give II (R = Bu; R1 = H; R2 = OH). The

latter, in CH2Cl2 contg. methylene blue, was irradiated while O was bubbled through the soln. to give I (R = Bu).

IT **150894-03-4P 150894-04-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antimalarial)

RN 150894-03-4 CAPLUS
CN Pyridine, 3-[(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl)methyl]- (9CI) (CA INDEX NAME)



RN 150894-04-5 CAPLUS
CN Pyridinium, 1-[3-(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl)propyl]-, chloride (9CI) (CA INDEX NAME)